THE Journal OF THE Kansas Medical Society

AUGUST
1961

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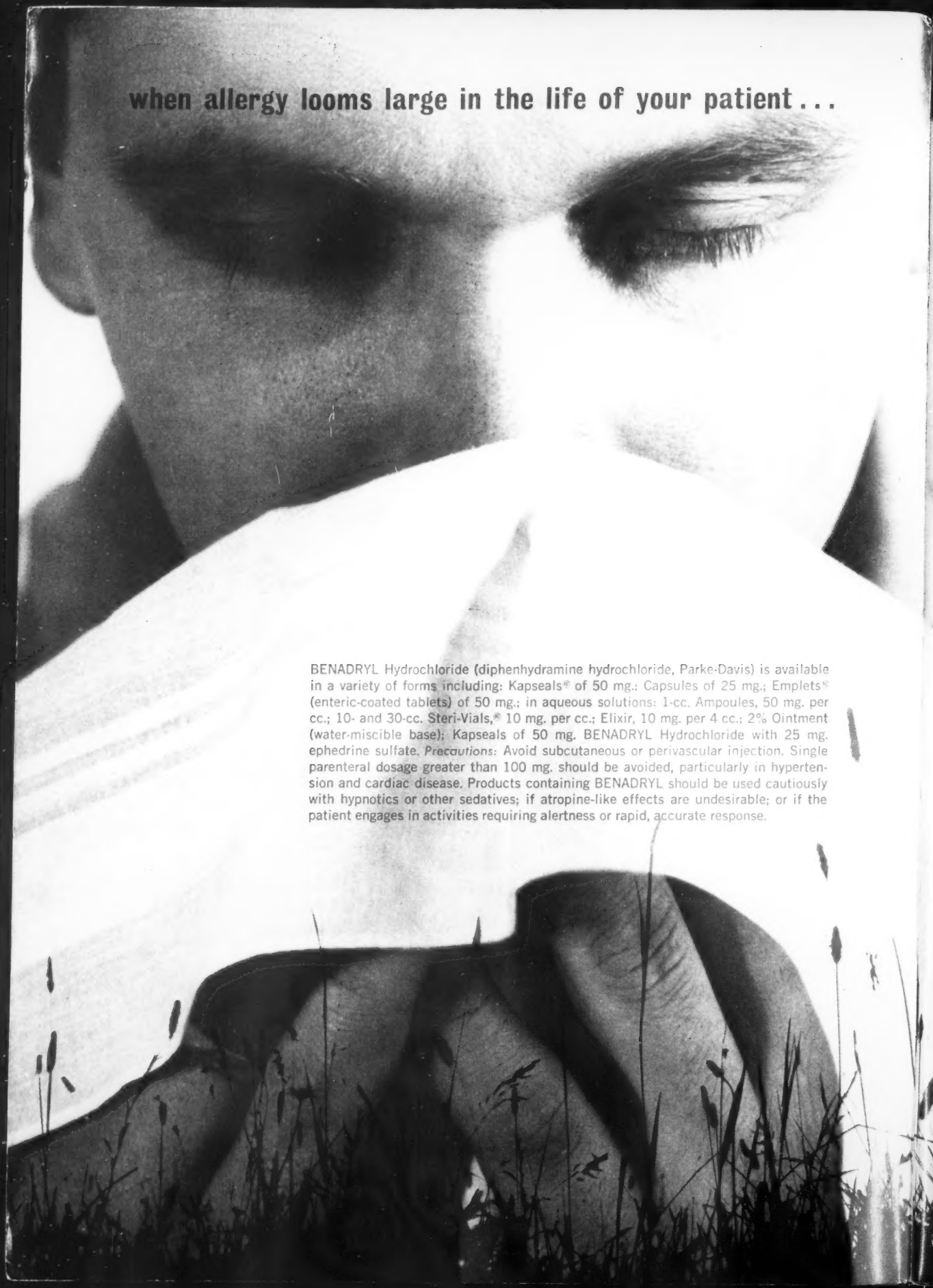

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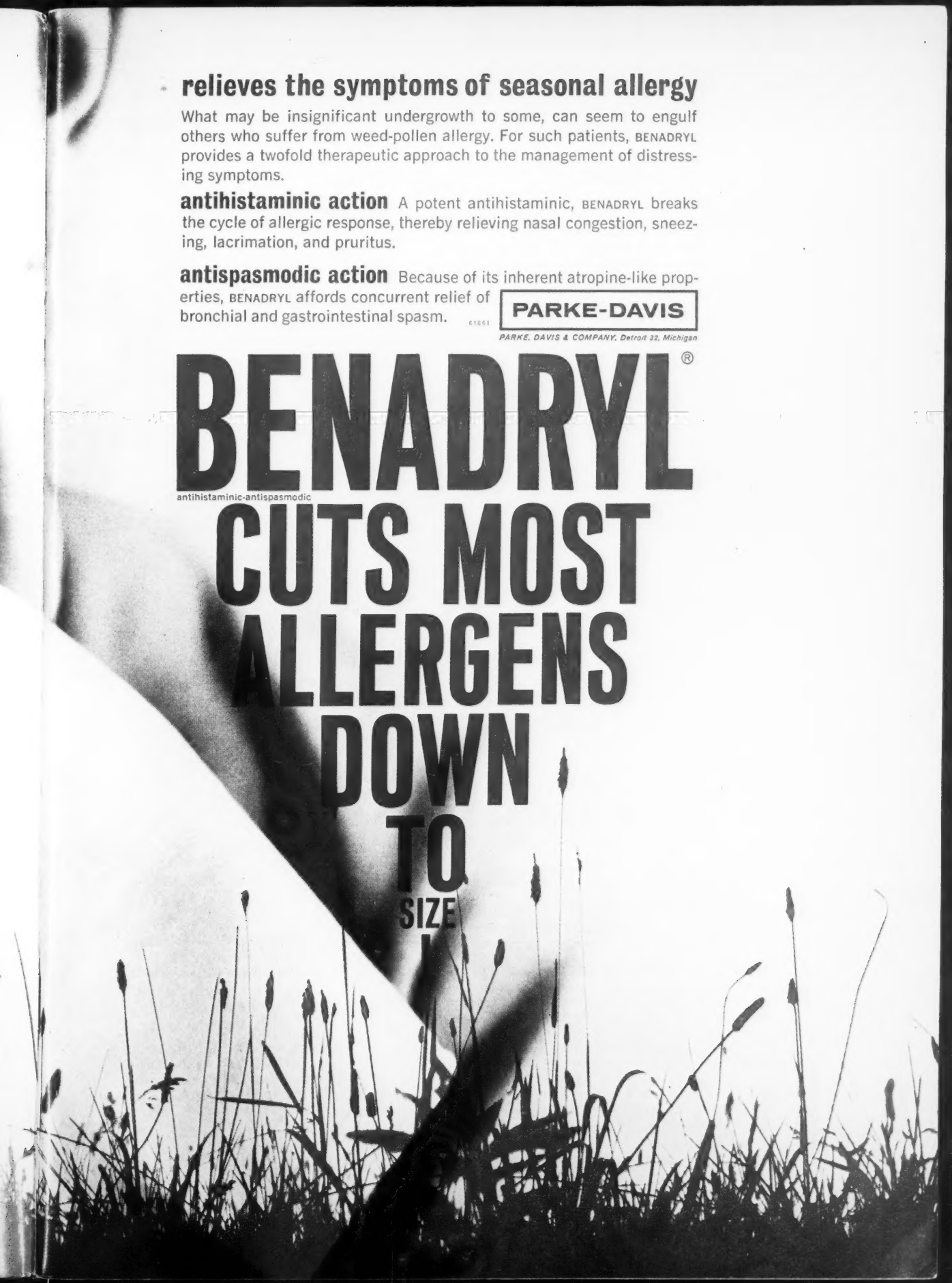
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Volume LXII, Number 8—August, 1961

The JOURNAL of the KANSAS MEDICAL SOCIETY

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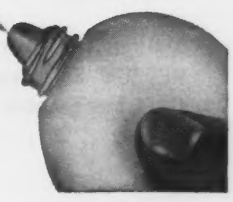

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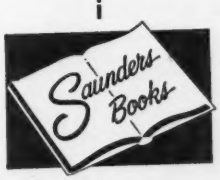

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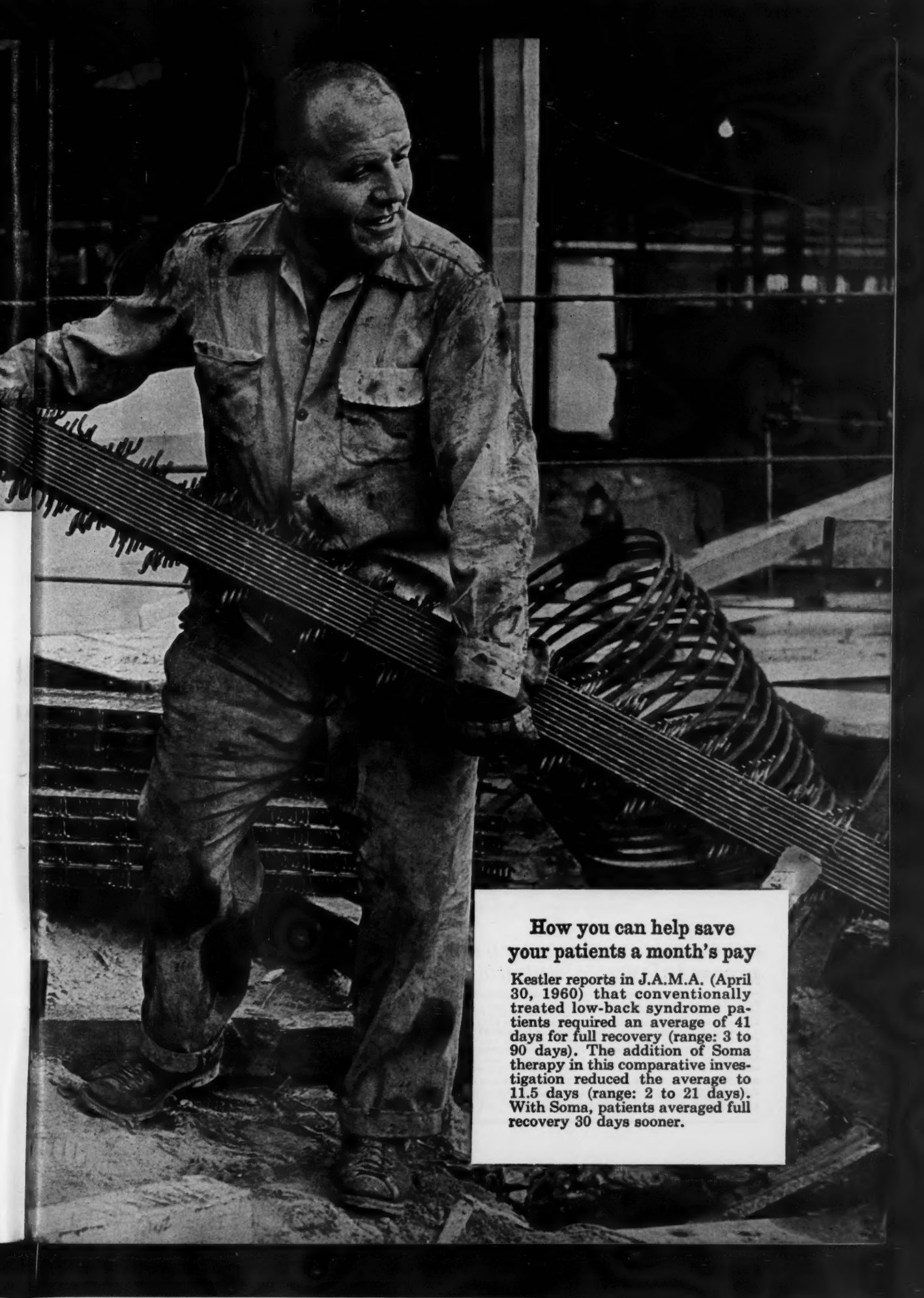

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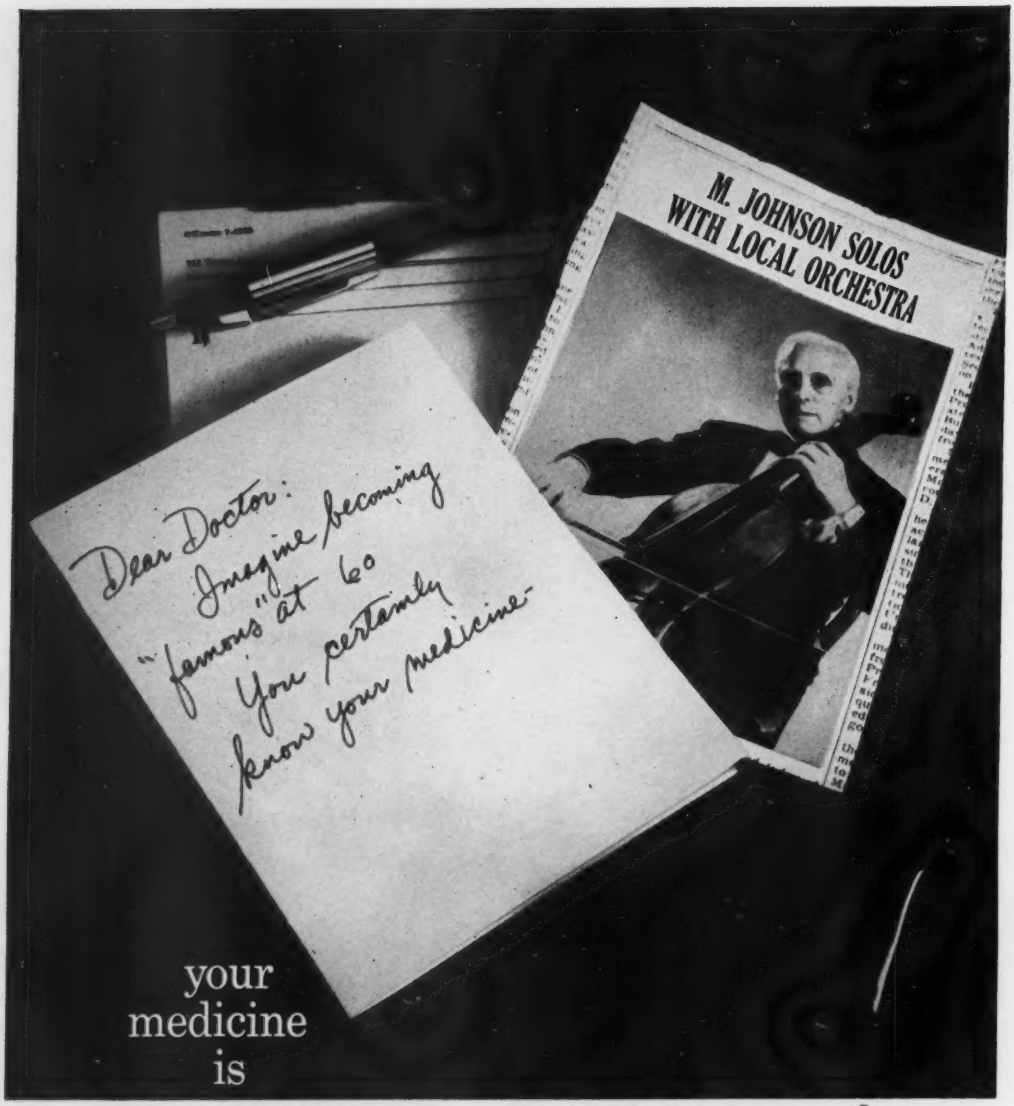

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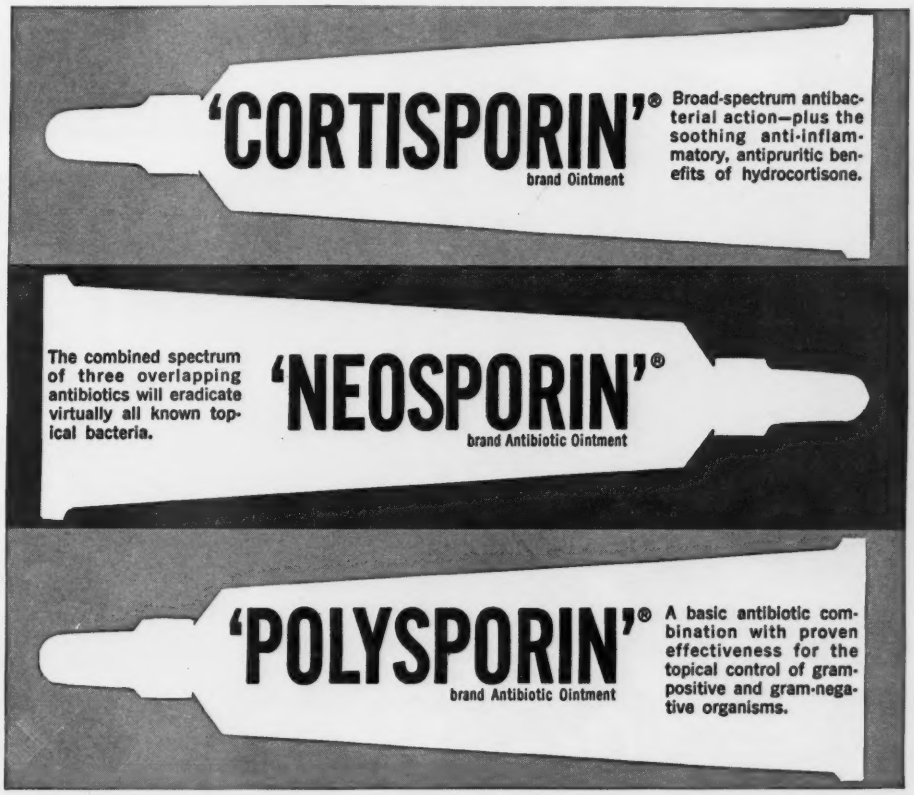
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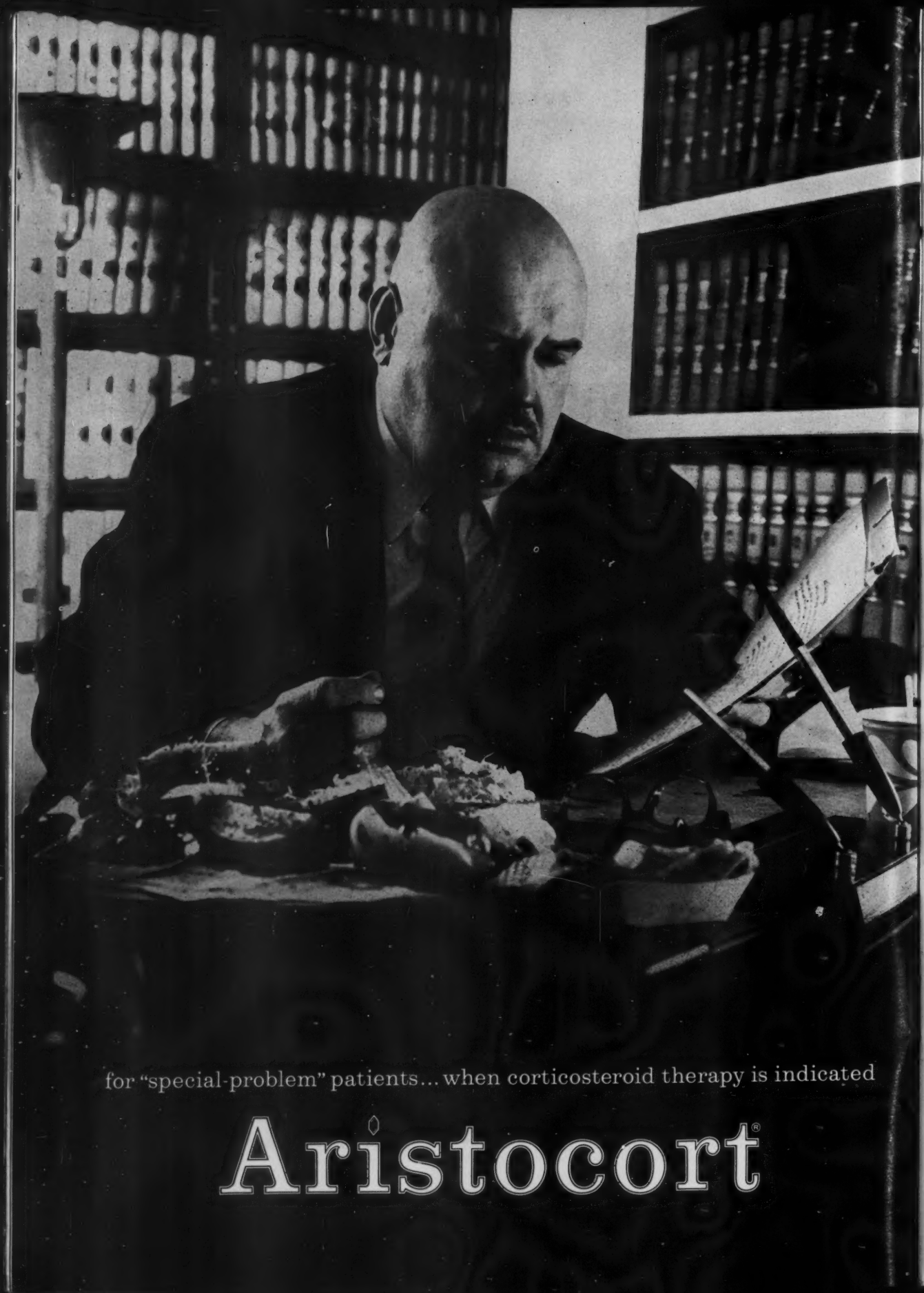

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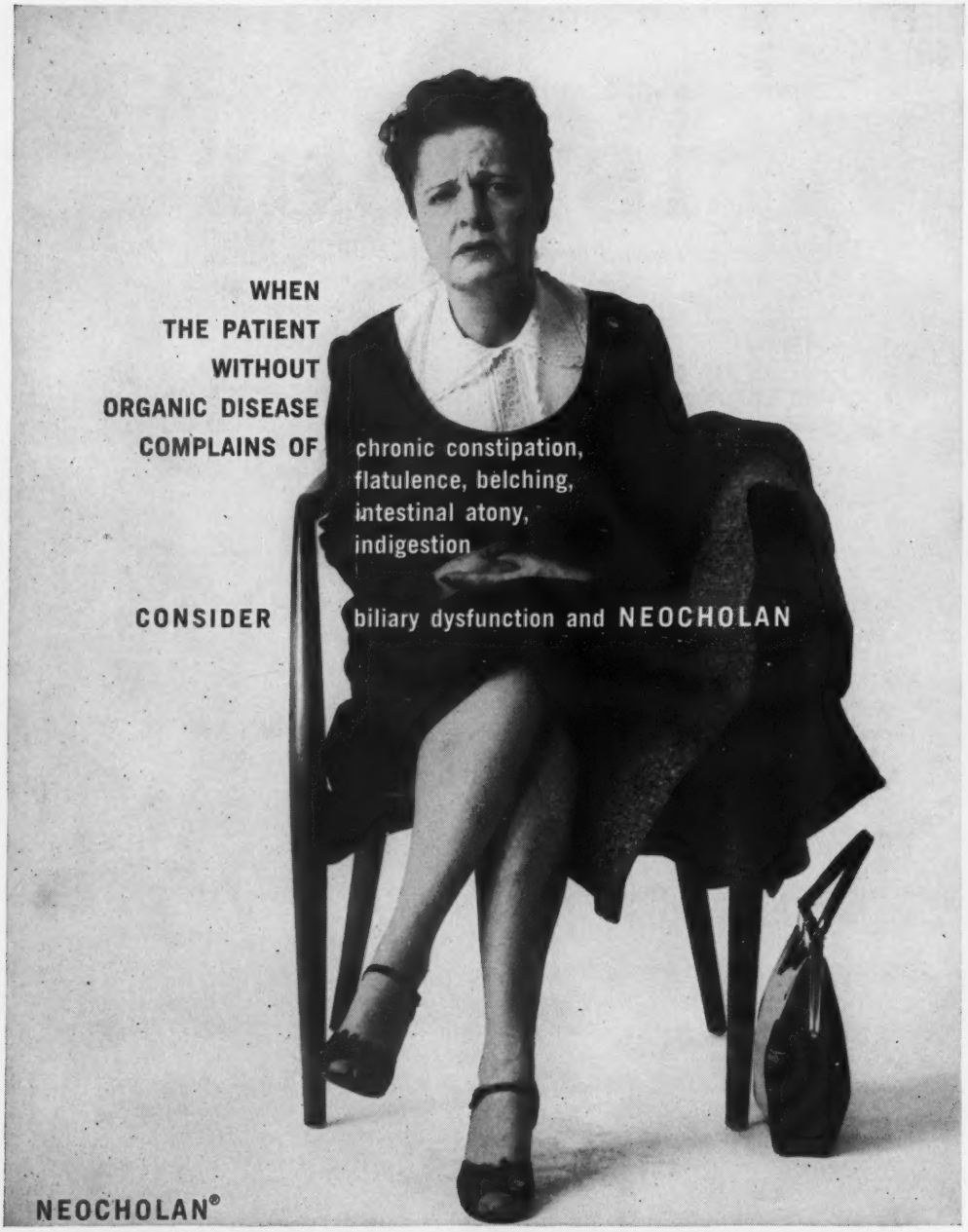

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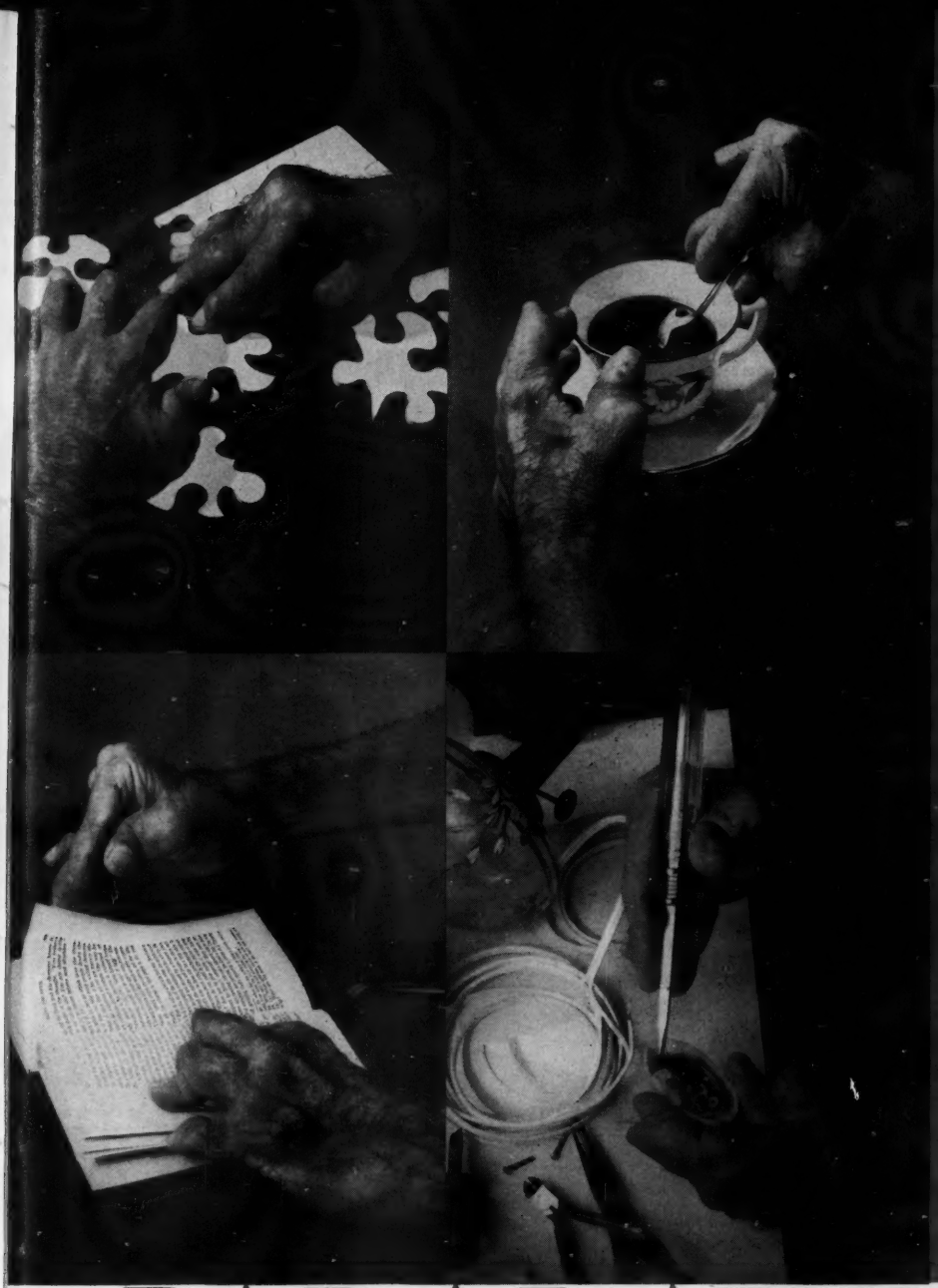

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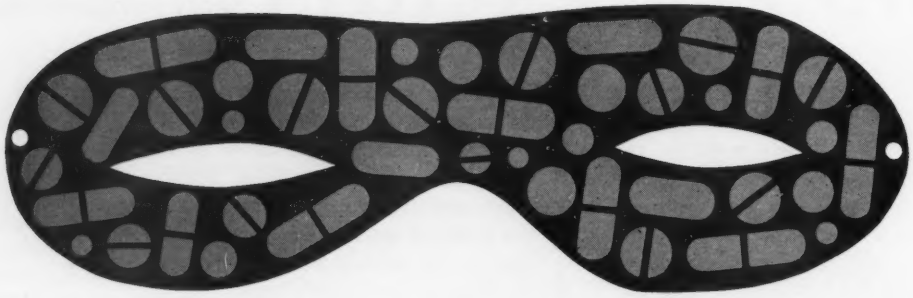

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Rhode Island Medical Journal,
January, 1961

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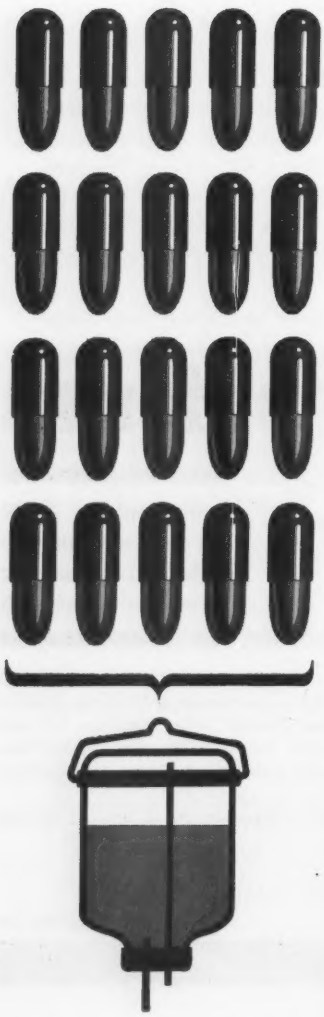

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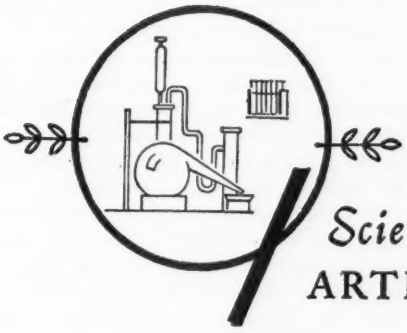

Scientific
ARTICLES

I^{131} Scannergrams

The Use of I^{131} Scannergrams in The Evaluation of the Thyroid Nodule

D. R. GERMANN, M.D., *and* ROBERT BURNS, M.D., *Kansas City*

RADIOACTIVE IODINE is a very popular and accurate test of thyroid function. It has also been used in an attempt to identify thyroid cancer. This is based on the finding of I^{131} outside of the thyroid areas. This would imply metastatic functioning thyroid gland.

Scannergrams of the thyroid gland offer a slightly different approach to the thyroid problem. By this means we are attempting to identify which portion of the thyroid gland functions normally or abnormally. If the site of abnormal function relates to a thyroid nodule this has some diagnostic significance. It is in this manner that we hope to study patients and eventually separate the surgical nodule from the non-surgical nodule.

Material

Between October 1953 and January 1960 approximately 22,000 radio-iodine uptake studies were done. Of this total 1,662 thyroid scanning procedures were done. The scanning procedure was limited to patients who had a palpable nodule or who had an elevated I^{131} uptake. There were rarely other indications for the scan. Of these scans only 106 patients came to surgery in our institution. Surgery was performed in other institutions for several patients but all could not be followed. For that reason all who were not operated upon at the K. U. Medical Center have been eliminated from our statistics. Eighteen cases of carcinoma of the thyroid were found in this group of patients which is approximately one-half the thyroid cancers registered at this institution during this period of time. Patients operated upon in the hospital without scans are not included in the statistics.

Method

The scans were made by a scanner which is one of the early commercial models (Tracer-Labs Tracer Scanner). The scintillator is a thallium-activated sodium iodide crystal 1 inch long, 1/4 inch in diameter. The Tungsten shield is cylindrical and rounded to a smooth dome at the distal end, providing shielding of 5/8 inch with a 1/4 inch diameter hole. The patient is given 40 to 80 microcuries of radioactive sodium iodide orally, and the scan is performed approximately twenty-four hours later. The patient's nodule or nodules are marked on the skin. The position is transferred to the tracing by identifying marks on the scan. Virtually all of the patients and scans have been done by a member of the staff. (DG) Instructions to the patient during the scan included restriction of swallowing except when the scanning tube is at one side or the other.

Classification

This study is primarily based on nodular glands. Nodules are classified as follows:

(A) Hyperfunctioning nodules reflect increased concentration of sodium iodide as compared to

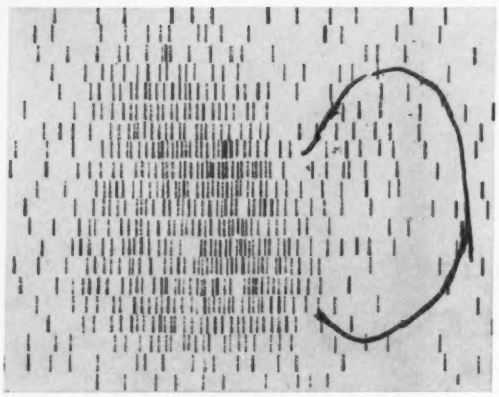

Figure 1

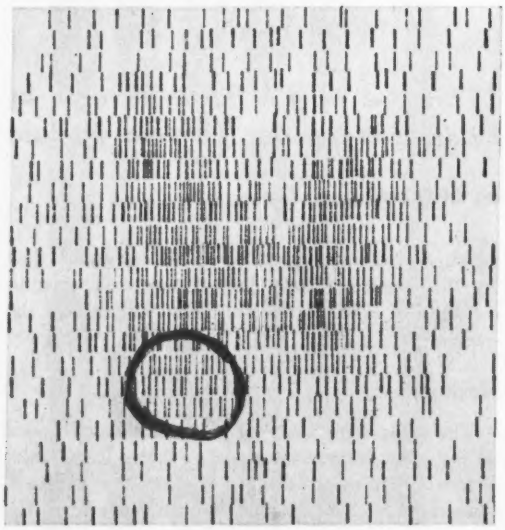

Figure 2

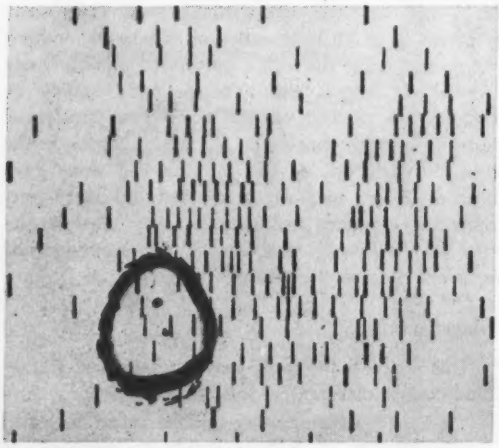

Figure 3

adjacent thyroid tissue. This is an exceedingly difficult situation to prove since a gland which is increased in its thickness, or mass, in a given area must be distinguished from a nodule.

(B) Functioning or neutral nodules represent an area in which the activity of sodium iodide is essentially the same as surrounding thyroid tissue, or the function of the gland does not appear to be altered by the presence of nodules.

(C) Reduced or non-functioning nodules or areas which are palpable and which show less function than the adjacent thyroid tissue. This is perhaps the easiest to evaluate since the increased mass may be present where there is decreased function. The following figures, 1, 2 and 3 are examples of each of the above classifications.

Results

Further classification of the results was possible by dividing the multinodular goiters from the solitary nodular goiters. The pathology report was used in making this division since it is occasionally difficult to be certain from the clinical findings. The results of solitary nodules are shown in Fig. 4. The results of multinodular goiters are shown in Fig. 5. Total summary of results are shown in Fig. 6. It will be noted that there is a strikingly high incidence of malignancy in the non-functioning solitary nodule.

Discussion

By auto-radiography, Dobyns,[1] suggests that the discreet capsulated nodules should be arranged histologically in a spectrum ranging from the least differentiated and progressing to the most differentiated pattern and that generally there was a parallel to function. Greene[2] analyzed a series of 202 cases of which 93 were functioning, and 109 were non-functioning nodules, by constructing isodose curves from auto-radiography. There were no malignant lesions in the functioning group. Groesbeck,[3] analyzed 527 patients of which 233 subsequently had surgery. Three carcinomas in the functioning nodular group and 20 of the 121 non-functioning group were found. Perlmutter,[4] reporting on 116 cases found 23 of 99 non-functioning nodules were malignant, and only one of 40 functioning nodules was malignant. This latter was an area of function in a metastatic node. Fig. 7 is a summary of the above mentioned cases plus our own statistics.

Conclusion

Our scanning device has been used over a seven-year period. During that time there have been many technical advances in this area. We have elected not to change our technique but try to be consistent in our studies. The above statistics would seem to sup-

SOLITARY NODULES—37 CASES

A. Non-function on Tracergram

Carcinoma	10
Non-carcinoma	15

B. No Alteration in Function

Carcinoma	0
Non-carcinoma	12

Figure 4

MULTIPLE NODULES—69 CASES

A. Non-function on Tracergram

Carcinoma	5
Non-carcinoma	55

(45 were colloid nodular)
(6 were Ch. thyroiditis)

B. No Alteration in Function

Carcinoma	0
Non-carcinoma	9

Figure 5

INCIDENCE OF CANCER IN SURGICALLY REMOVED NODULES

	Incidence Per Cent
Total of 15 cases out of a total of 106	14

INCIDENCE OF CANCER IN NODULES WITH DIMINISHED FUNCTION

Cases	*Incidence Per Cent*
Sol. Nodule—10 out of 25 cases were Ca.	40
Mul. Nodules—5 out of 60 cases were Ca.	8

Figure 6

Source	*Isotope Classification*	*Pathologic Classification* B	CA	*Total*
Perlmutter and Slater	Cold	76	23	
	Hot	40	1*	140
Groesbeck	Functioning	80	3	
	Non-functioning	121	20	
	Hyperfunctioning	13	0	237
Greene	Cold	109	22	
	Neutral or hot	93	0	202
KUMC	Non-functioning	85	15	
	Functioning	21	0	106
				685

Figure 7

port the basic premise that a thyroid nodule which functions has a very low probability of malignancy, and that a thyroid nodule which does not function should, in general, be considered a surgical nodule.[5] This is particularly true if the nodule is a solitary one.

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Editor's Note: This article was submitted to THE JOURNAL for publication in March, which is the University of Kansas Medical Center issue. Due to space limitations at that time, THE JOURNAL was able to publish only half of the articles submitted.

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Life's Depths

The depths of life are spiritual depths. They are are not gained by travel, be it ever so wide, nor by exciting worldly adventures. They are plumbed at home, by the fireside, at the supper table, in bed on sleepless nights, in the snatched intervals of exhausting and ordinary toil, in the room where a father lies dying, in the room where two young people are confessing love, in the room where a child is born.

—Author unknown

Superstitions

Do rats desert a sinking ship? According to a mammalogist at the New York City Museum of Natural History—if they do, it's only because they're holed up in the bottom of the ship and want to get out. Who wouldn't?

Schizophrenia, the nation's number one mental disorder is recognized most frequently during the most productive years of life, according to *Patterns of Disease,* a monthly Parke, Davis & Company publication for physicians. A study of patients admitted with the disease to nonfederal mental hospitals showed that the highest incidence of the disease is in the 25-34 age group.

The Heart and Surgery

A Statistical Analysis of Cardiac Output During and Following Surgical Operations

ALFRED HEILBRUNN, M.D.,* ***and***
WILLIAM SEEMAN, PH.D.,** ***Kansas City***

THE CARDIAC INDEX DATA to be presented and analyzed in this paper were obtained in the course of a study carried out at the University of Kansas Medical Center. The clinical characteristics of this study are described in considerable detail elsewhere: the subjects, the apparatus, the method, and some clinical aspects of the study findings.[1] It is our purpose in this paper to present a statistical analysis not elsewhere presented.

Briefly, the changes in cardiac output preceding, during, and following operation were studied in a group of unselected patients. The method used was the indicator dilution technic. This method employs the introduction of a known quantity of indicator agent into the blood stream as a bolus and the measurement of its concentration following initial passage through the heart and lungs. From this determination and the time of passage, the dilution of the indicator, and hence the blood flow through the heart and lungs, can be calculated.[2]

Table 1 presents the cardiac index data for ten patients under the five different conditions. There were twelve patients in the original study, but for two of these twelve patients the data were missing from one or another of the conditions. The data for these two patients were therefore not included in the analysis. Where more than one reading was obtained for any patient the mean was computed as a more precise measure of the variable. The figures in parentheses indicate the *rank* order of the measure obtained; i.e., the lowest measure for each patient is assigned a rank of one, the next a rank of two, etc. Since there were five different conditions under which measures were derived for each patient, these measures are ranked in the table from one to five. The reason for assigning these ranks will be discussed below, in connection with the statistical analysis.

Table 2 presents the analysis of variance data derived from the original data in Table 1. The F ratios are both significant at the .01 level of confidence. This indicates, first, that the measures derived under the different "treatment conditions" (i.e., the different conditions under which the measures were obtained—e.g., B, PI, etc.) are reliably different; which is to say that the differences attributable to these varied conditions are too great to be accepted as "chance" differences, and are properly to be considered as "real" differences, brought about *not* by chance fluctuations of the measures but by the conditions themselves. Table 2 indicates, secondly, that the differences from individual to individual for the ten patients in the study are also reliable and real differences, and again are not attributable to chance fluctuations in the cardiac index measures. To summarize: The measures are reliably different for both the different *conditions* and the different *patients*.

Data on the cardiac index under a variety of specified conditions are analyzed. The results of this analysis indicate that there are statistically reliable differences between individuals and between certain of the conditions.

The analysis of variance test indicated in Table 2 is one of the more powerful of the statistical tests available, and it is for this reason that the particular statistical technic was applied. It requires, however, some knowledge of the way in which cardiac index measures are distributed in the general population; and more specifically, it assumes that the distribution follows the normal curve (bell-shaped curve). Assuming that cardiac index measures are, indeed, distributed in this way, the use of the analysis of variance technic is appropriate. However, a second assumption involved is the assumption that the standard deviations are also comparable for the different "treatments" and for the different individuals or patients. To protect against any error which might derive from a failure to meet this condition, we chose to submit the data to another type of analysis, using this time, a non-parametric statistic; i.e., one which is less powerful but which makes no assumptions concerning the way in which these measures are distributed in the general population. For this test the data need to be converted to ranks, and the analysis of the ranks provides the statistical test. It is for this reason that the original data in Table 1 were con-

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** Department of Psychiatry, University of Kansas School of Medicine.

TABLE 1

CARDIAC INDEX FOR TEN PATIENTS UNDER CONDITIONS BEFORE SURGERY (B), POSTINDUCTION (PI), DURING PROCEDURE (DP), RECOVERY ROOM (RR), AND POSTOPERATIVE (PO)

Case No.	*B*	*PI*	*DP*	*RR*	*PO*
1	3.04(4)*	2.01(1)	2.14(2)	3.07(5)	2.85(3)
2	2.71(4)	1.83(1)	2.00(2)	2.14(3)	3.31(5)
3	4.45(5)	3.28(1)	3.65(2)	4.37(4)	3.94(3)
4	4.24(3)	2.99(1)	3.87(2)	4.19(5)	4.34(4)
5	3.66(4)	3.73(2)	3.26(1)	4.99(5)	3.36(3)
6	3.27(4)	2.31(2)	2.59(3)	1.68(1)	4.11(5)
7	2.65(2)	2.42(1)	3.61(5)	3.44(4)	3.40(3)
8	3.05(4)	2.22(1)	3.01(3)	4.68(5)	2.89(2)
9	4.04(5)	3.03(1)	3.33(3)	3.80(4)	2.92(2)
10	4.18(4)	2.66(2)	2.38(1)	4.41(5)	3.64(3)

* Numbers in parentheses indicate rank order of the cardiac index values under the different conditions. E.g., for Case No. 1, 2.09 (PI) is the lowest value, 2.14 next, etc. These rank values are used in the non-parametric analysis indicated below.

TABLE 2

ANALYSIS OF VARIANCE

Sources of Variation	*Sum of Squares*	*Degrees of Freedom*	*Variance*	*F Ratio*
"Treatments" (B, PI, etc.)	8.243	4	2.061	6.40*
Individuals	14.710	9	1.634	5.07*
Remainder	11.619	36	.322	
Total	34.572	49		

* Significant beyond .01 level.

(NB. The purpose of this analysis of variance technique is to determine whether there is an *overall* difference among several sets of measures. The greater the differences among conditions and individuals, the larger the figures in column 2. Column four figures are obtained by dividing column two by column three figures. The F ratio is designed to tell whether the variation (i.e., differences) attributed to conditions and to individuals are significantly greater than *chance* variations, as represented in the remainder. Consequently, the F ratios in the last column are obtained by dividing each of the variance figures in column four by .322. The statistical significance of these values for F is then determined by consulting the appropriate table of F values.)

verted to rank order. It turns out that with our data the X^2_r (the statistic for the analysis of variance of ranks) is 21.44; and the tabled value for the statistic indicates that this is beyond the .01 significance level. It therefore seems quite safe to claim that we have demonstrated real differences over the conditions and the patients.

Having established these two kinds of differences, we next ask the question: Are there some conditions for which the measures are more "alike" than for other conditions? The analysis designed to answer this question is presented in Table 3. The statistic used here is the Wilcoxon Matched Pairs Test. This table suggests that we may be most confident about the differences between B and PI conditions, between PI and PO conditions, and between PI and RR conditions. On the other hand, these Wilcoxon values indicate that we have not demonstrated differences in the following: between B and RR conditions, between B and PO conditions, between DP and PO conditions and between PO and RR conditions.

TABLE 3

DISTRIBUTION OF WILCOXON T VALUES FOR DIFFERENCES BETWEEN CARDIAC INDEX VALUES FOR DIFFERENT SPECIFIED CONDITIONS

	B	*PI*	*DP*	*RR*	*PO*
B		1**	9†	23	25
PI			10.5†	2**	3**
DP				6.5*	10
RR					17

** Indicates highly significant difference (.01 confidence level).

* Indicates significant difference (.05 level).

† Barely misses level of statistical significance.

Summary

We have presented in this paper a statistical analysis of data on cardiac output in surgery, in the recovery room, and under postoperative conditions. The method employed was the indicator dilution technic. The analysis of variance statistic indicates a reliable difference in cardiac output for the five conditions described in the paper. The statistical analysis also indicates significant differences in cardiac output from patient to patient. The Wilcoxon matched pairs statistic was used to indicate which of the five conditions could be considered as "most different."

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Carcinoma of the Liver

A Report on 31 Cases

COLVIN H. AGNEW, M.D.,* *Kansas City*

PRIMARY HEPATIC NEOPLASMS have been positively diagnosed in 31 patients in this hospital during the past decade. The most unique feature in this series has been the high incidence of children (8/31). My attention became focused upon this disease in Kansas when two children (cases 3 and 4) were referred within a short period of time for radiation therapy. An account of the pediatric group is being prepared. Approximately 10,000 malignancies have been registered here during this time. This figure includes approximately fifty cases of carcinoma of the gall bladder and common bile duct. Thus, we are dealing with a rare tumor even in a teaching hospital. Hepatic cancer is notably more common in certain groups in their native habitat (Bantu and Oriental).[1, 4, 6] This small series has shown many of the features recorded in larger series.

Material

The clinical records have been reviewed on eight children and 23 adults. The sex and race by age distribution are summarized in Table I. It is curious that no Negro children are included. There is a general 2:1 preponderance of male over female patients.

Diagnosis

The diagnosis was established from tissue acquired either at exploratory laparotomy or at autopsy, except case 27 (needle biopsy). The diagnosis is that registered by the pathologist reporting on the material. It is summarized in Table II.

The inherent perplexity in microscopic diagnosis is reflected in case 13 (WB). A needle biopsy was interpreted as representing a hemangioblastoma; however, at autopsy the diagnosis was changed to carcinoma predominantly bile duct type with cirrhosis.

The difficulty of establishing the primary site of origin is represented in Case 21 (IB). At surgery it was felt that this patient had a primary pancreatic tumor with hepatic metastasis. The surgeon performed a Roux-Y operation. It later developed that this patient had a primary liver cancer (large cell type).

Classification

Edmonson and Steiner[4] advocate the terminology "liver cell carcinoma" and "bile duct carcinoma." These terms have essentially the same meaning as the terms chosen by Berman, "hepatocellular carcinoma" and "cholangiocellular carcinoma." This series has been classified according to this terminology. The numerous synonyms for these two types of cancer have been included *(Table II)*. Edmonson and Steiner review the problem of classification and justify their choice. To a non-pathologist this system has appeal and much to recommend its use.

Thirty-one cases registered in the past decade have been reviewed. The material has been reviewed primarily to study the effect of therapy upon life expectancy. The only specific therapy that has been really effective is surgery. One case appears to be alive without disease. One child seems to have been remarkably benefited by nitrogen mustard. Indications for radiation therapy are not clear. Eight children are in this series. Their inclusion has not seemed to alter the data.

Pathology

Experienced liver cell pathologists are able to divide primary liver cancer mainly into two groups: Liver cell cancer and bile duct type cancer.

Grossly these livers frequently have multinodular surfaces, but may retain their hobnail appearance. Upon cut section the surface may reveal various sized nodules of varying colors from gray to the more normal light brown (liver color). As the intrahepatic lesions replace normal hepatic cells, the fibrous septa may be retained, yet producing enlargement of the liver through gross intra-portal invasion.

Microscopically irregular cords of tumor cells crowd adjacent liver parenchyma. These cells merge almost imperceptably with uninvolved cells. It would be inappropriate to pursue the microscopic distinction between the two major cell types. However, in the more well differentiated cases the large polyhedral cells resemble normal hepatic cells in the liver cell type. In the bile duct type there is an adenomatous

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formation which is usually distinguished from the liver cell type.

Clinical Course

An upper abdominal mass present for one to three months occasionally associated with ascites, and an insidious upper abdominal discomfort or pain were regularly present. Jaundice was rare. Abnormal physical examination was usually confined to the enlarged liver. The x-ray film often revealed an elevated right hemidiaphragm, hepatomegaly, and occasionally pulmonary metastasis. The laboratory data usually did not show any abnormal findings unless the cirrhosis was quite severe or obstructive jaundice was present.

After the diagnosis treatment was usually symptomatic. Excision possibly contributed to the control in Case 23 (RT). Usually nitrogen mustard and radiation were not of value. Nitrogen mustard apparently has contributed significantly to the survival of case No. 1 (JB). Eighteen months after treatment she is well, attending school, and gaining weight; however, the liver is slowly enlarging. Shrinkage of the liver neoplasm was observed in cases 4 (RP) and 8 (FL). Supportive therapy frequently included salt restriction, cortisone, bed rest, improved diet and vitamin K. Most of the patients died within three months from the time the diagnosis was established.

Three clinical examples will be given in summarized form to emphasize the clinical courses.

Short Time Survivor With Responsive Tumor

Case 8. Nine days after birth this male infant developed "swelling of the abdomen." Two weeks before admission he developed a fever and continued with daily temperature elevations despite antibiotic and aspirin therapy. He had a protuberant abdomen, and the liver was palpable six fingers below the right costal margin. After the liver biopsy, he was treated with 250 KV x-radiation (2,000 rDn/15 days), Meticorten 5 mgm. t.i.d. and Achromycin 250 mgm. daily. The liver markedly decreased in size during the radiation. The swelling in the lower extremities gradually disappeared. However, 15 days after radiation was started and after temporary abdominal improvement, vomiting became a serious problem. Two days later ptosis of the left upper lid was noted. He lived another 15 days on supportive therapy.

Comment: This patient exhibited local response to radiation which in our experience is unusual. He apparently died of intracranial metastasis. He had an osseous metastasis to a tibia demonstrated by x-ray film. This was not treated.

Short Course Without Response

Case 9. Two months before admission, this 20 year old Negro noted a feeling of fullness in his abdomen after eating, and lost 25 pounds. He became aware of a right lower quadrant mass. One month before admission, he was seen elsewhere and told that he had an enlarged liver and "spots on his lungs." Abdominal examination revealed a huge nodular liver extending to the iliac crests. After liver biopsy he received radiation to the liver (2,000 rDn/50 days). Improvement was not noted. There was a steady deterioration in his condition with the terminal development of an obstructive jaundice. He was afebrile.

Comment: Except for the youthfulness of this patient he represents a rather typical patient and course. He was a well individual until three months before his death, when he noted a vague abdominal discomfort and an abdominal mass; at that time he had advance secondary deposits. The treatment was without benefit.

Unusually Long Survivor

Case 23. This 59 year old Negro housewife was first seen at the Medical Center in 1954, complaining of right upper quadrant pain for five years and an abdominal mass for two years. She had been seen at the Mayo Clinic in May, 1950, and it was their opinion at that time that the upper abdominal mass was most likely an anomalous lobe of the liver and did not advise surgery. In 1954 (after being advised here) to have surgery, an exploratory laparotomy was performed in November, 1954, at St. Margaret's

TABLE I

Age	*14*	*15-29*	*30-39*	*40-49*	*50-59*	*60-69*	*70-79*	*80*
Sex	M F	M F	M F	M F	M F	M F	M F	M F
W	5 3	1 0	0 1	1 0	1 2	3 1	4 1	1 0
N	0	1	0	0	1 1	1 1	1 0	0 0

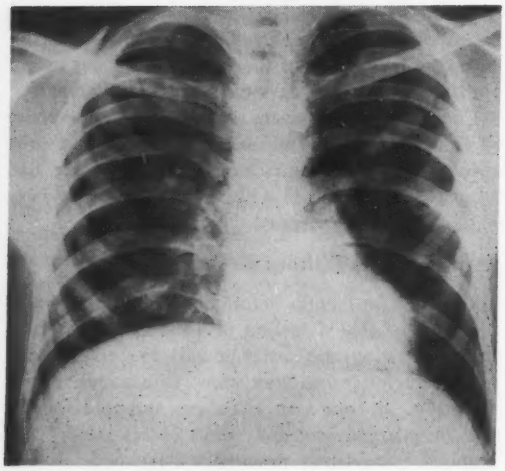

Figure 1. Case 9. Multiple pulmonary metastases were present when first seen.

Hospital with partial hepatectomy and cholecystectomy.

Her next hospital admission (KUMC) April 1958 revealed a recurrence of the right upper quadrant mass; her chief problem, however, was congestive heart failure. She was treated symptomatically until her death November 7, 1959.

Comment: This intriguing patient represents one of the few well documented long survivors. The tissue was reviewed by several pathologists. Steiner and Higginson classified this lesion as a hepatocellular carcinoma. Steiner made the additional comment that he had seen one other case which had survived nine years following left lobe resection succumb with recurrence.

TABLE II

	Male	*Female*	*Total*
Liver cell carcinoma ...	15	7	22
(Hepatocellular carcinoma, hepatic cell carcinoma, trabecular carcinoma, hepatoma, malignant hepatoma, carcinoma simplex, carcinoma solidum, hepatoblastoma.)			
	Male	*Female*	*Total*
Bile-duct type	3	2	5
(Cholangioma, malignant cholangioma, cholangiocellular carcinoma, adenocarcinoma, duct cancer, alveolar carcinoma, carcinoma adenomastosum, columnar cell carcinoma.)			
	Male	*Female*	*Total*
Mixed	1	0	1
(Duplex, intermediate, carcinoma of dual origin, cholangiohepatoma, combined cell type, hepatobiliary carcinoma.)			
	Male	*Female*	*Total*
Sarcoma	2	1	3*
(Liposarcoma, case No. 3, case No. 7.)			

* Case 7. Anaplastic tumor in regenerated fibrotic liver.

Discussion

The outstanding feature of this disease is the inexorable downhill course. Most accounts of the clinical course indicate that death occurs within three months following the onset of symptoms for hepatocellular carcinoma and six months for the bile duct type carcinoma. There are two notable exceptions in this series. One has been presented in a brief summary. Case 29 (AM) had one-third of the liver removed. This patient is alive and well more than two years after surgery. This could represent a cure.

Figure 2. Case 4. Metastases to the spinal cord appeared 3 months after hepatic radiation had been completed.

CLINICAL MATERIAL

Case	*Age, Sex, Race*	*Diagnosis*	*Duration S/S Before Treatment*	*Treatment*	*Effect of Treatment*
1 JB	14 WF	Hepatic	Mass 3-4 months	HN_2	+18 months well; mass enlarging
2 CK	3 WF	Hepatic	Mass 1 month	Exploration	Died 4 hrs. after surgery
3 MP	10 WF	Fibromyxoma Sarcoma	Mass 2 months Precocious puberty	Radiation: 3000 rDn/24 days; HN_2	Died 4 months after treatment
4 RP	3 WM	Hepato-blastoma		Radiation	History abstracted
5 DD	2 WM	Hepatic	Gradual enlarge-ment	Vit. K	Died 1 month
6 JH	1 WM	Hepatic	Mass 1 month	Partial hepatectomy Radiation: 3100 rDn/34	Died 5 months
7 RK	1 LWM	Sarcoma	Mass 3 months	None	Died present admission
8 FL	6 wks. WM	Hepatic	Mass	Radiation: 2000 rDn/15 days	Died 15 days
9 JP	20 CM	Hepatic	Fullness 2 months	Radiation: 2000 rDn/50 days	Died 1 month
10 MM	33 WF	Hepatic	Pain RUQ 5 months	None	Died 3 months
11 RC	44 WM	Hepatic	6 months chest pain	Exploration	Died 1 day after surgery
12 LO	53 WM	Hepatic	Pain RUQ duration vague	HN_2 portal vein	Died 5 months
13 WB	59 CM	Bile duct type	Ascites duration vague	None	Died 1 week
14 MW	56 WF	Hepatic	RUQ mass 18 months	None	Died 2 months
15 VP	50 WF	Bile duct type	Jaundice 2 months	Radiation advised	Died 5 months
16 NM	59 WM	Hepatic	Mass duration 2 months	Dietary	Died 2 months
17 NM	51 CF	Mixed type	Mass one month	None	Died 5 months
18 ES	68 WM	Bile duct type	Weakness 4 months	None	Died 1 month

CLINICAL MATERIAL—Continued

Case	*Age, Sex, Race*	*Diagnosis*	*Duration S/S Before Treatment*	*Treatment*	*Effect of Treatment*
19 WM	69 WM	Bile duct type	1 year epigastric dis.	Dietary	Died 2 months
20 HS	65 WM	Hepatic	Jaundice 3 months	None	Died 3 months
21 FF	67 CM	Hepatic	Admitted in coma	None	Died 24 hours
22 IB	61 WF	Hepatic	Mass 3 months	Roux-Y	Died 2 months
23 RT	64 CF	Hepatic	Mass 3½ years	Partial hepatectomy	History abstracted
24 WM	71 WM	Hepatic	Mass 4 months	None	Died esophageal bleeding
25 FG	76 CM	Hepatic	Mass 3 months	None	1 month
26 RS	71 WM	Hepatic	Mass 2 weeks	None	Died two weeks
27 AK	76 WM	Hepatic	Swelling	HN_2 portal vein Cortisone, chlorambucil	Died 3 months
28 AA	72 WM	Liposarcoma	Mass 6 months	Radiation: 2000 rDn HN_2	Died 2 months
29 AM	71 WF	Hepatic	Mass 8 months	1/3 liver removed	Alive and well 2+ years
30 FS	73 WF	Bile duct type	Gall bladder trouble—6 months	None	Died 2 weeks
31 PM	81 WM	Hepatic	Discomfort—duration vague	None	Died 5 months

Radiation has been conspicuously unsatisfactory in this series. Even when reduction in liver size was observed, clinical improvement was only temporary. This experience is in sharp contrast to the value of radiation cited by Phillips.[9] It is worth noting that Phillips recommends higher doses than were usually given in this institution. It is perhaps important to note that his series (as pointed out by him) was unique in several respects. Perhaps radiation is indicated in those patients who have had a longer history before diagnosis.

The potential value of the operative cholangiogram has not been previously emphasized. The film on one patient on whom cholangiography was done was not available for review; the report, however, describes intrahepatic obstruction which might be anticipated. The information contributed by this method may provide prognostic data.

The difficulty in making the diagnosis either at surgery, by needle biopsy, or biopsy material obtained at exploratory laparotomy has been emphasized by others. Examples have been cited which typify the difficulty of diagnosis encountered in incomplete anatomic studies. Higginson,[7] on the other hand, em-

phasizes that it is a valuable method of diagnosis, particularly in an endemic area.

As in most series, cirrhosis was the conspicuous feature. The association of cirrhosis and liver cancer has prompted numerous speculations.[4, 5, 8, 11] Many have seized the opportunity to rationalize along the line that the regeneration opens a pathway to chaotic cellular proliferation. Higginson suggests that infectious hepatitis rather than racial history or dietary habits may be an important factor in the development of cirrhosis.[8] It should be mentioned, however, that only a small proportion (less than 5 per cent) of livers showing Laennec's cirrhosis also have cancer. On the other hand, Roth and Duncan[11] reported upon the occurrence of a primary carcinoma after giant cell hepatitis of infancy. The possibility of a virus hepatitis in an especially susceptible population with perhaps hyper-response of regeneration has been suggested.[8] Despite a century of study the association of cirrhosis and primary cancer of the liver leaves many unanswered questions.

Functional hepatic tumors are apparently quite rare. Reeves, *et al.*,[10] described an eight year old boy with precocious puberty associated with a hepatoma, who died about seven months after diagnosis. A recent clinical pathologic conference (Case No. 46451)[3] at the Massachusetts General Hospital described a case in a two year old boy who was treated with actinomycin D and estrogen. He died about three months after exploration. Our Case No. 4 (RP) was similar; he did have a somewhat longer clinical course.

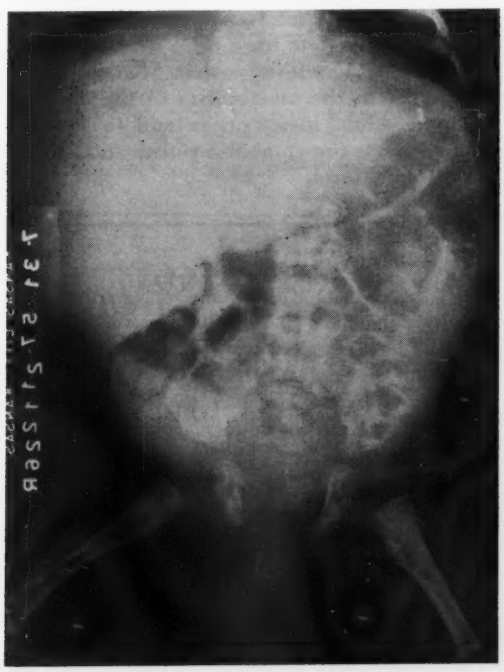

Figure. 3. Hepatomegaly was commonly present displacing colon downward and elevating right hemidiaphragm.

The importance of distinguishing between liver cell carcinoma and bile duct carcinoma may be of more than academic importance. Edmundson and Steiner have shown that the life expectancy is doubled in bile duct type. The series is too small to make a significant observation in this regard. The missing cell type of origin in previous series has been supplied by Steiner and Higginson.[12] Their description of a liver tumor arising from cholangioles completes the anticipated cell type. This series includes three sarcomas, Case 3, a fibromyxosarcoma, Case 7, "sarcoma," and Case 28 a liposarcoma. Their inclusion has not been an oversite; their clinical course was essentially the same as tumors that have derived from the epithelial liver elements.

It is my understanding that no estimate has been made of the relative number of cells at risk, i.e., whether the present ratio between liver cells, bile duct cells, and cholangiocellular carcinomas reflects the ratio of normal parent cells at risk. The important question raised by Higginson is, what is (are) the factor (s) responsible for the disproportionately higher ratio of liver cell to bile duct carcinoma between the Bantu and metropolitan U. S. A. Citizen? The ratio in males of bile duct type cancers is given[9] as 2.9:2.3 while the ratio between liver cell type cancer was 106.3/11.4. Thus, it has a bearing upon the etiology and raises the hope that there may be a preventable factor (s) in the Bantu environment.

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(Continued on page 361)

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Cholesterol

The Metabolism of Cholesterol in the Central Nervous System

HAROLD J. NICHOLAS, Ph.D.,† *Kansas City*

THE ADULT CENTRAL NERVOUS SYSTEM contains one of the largest concentrations of cholesterol in the animal body. Yet this large mass of sterol is singularly different from cholesterol in most other tissues* in that it is metabolically inert, i.e., it undergoes no turnover. It seems probable that the purpose of this metabolic inertness lies in the function of central nervous system cholesterol as a structural unit of the myelin sheath. However, this assumption does not afford any clue to the basic reason for the lack of turnover. Why should this particular mass of sterol remain segregated from the metabolic forces which keeps other cholesterol body pools in constant activity?

The first real insight into the biochemistry of brain cholesterol came from the observations of Waelsch *et al.*,[2] who fed and injected deuterium-labeled H_2O to adult rats and found appreciable deuterium in cholesterol of all organs examined except the brain. Similarly, when D_2O was fed and injected into a pregnant rat and into the newborn animals, deuterium was found in cholesterol of all young rat tissues examined, including brain.[3] Since D_2O is freely permeable to the blood-brain barrier, there was no question in these experiments that the label was available to every organ. It was concluded that in the young brain, cholesterol is actively metabolized whereas in the adult organ cholesterol metabolism ceases or exists at a very low level. Labeled acetate given intraperitoneally to an adult rat produced no labeled brain cholesterol.[4] The possibility of the acetate not passing the blood-brain barrier seems not to have been considered in this experiment, which therefore has no valid interpretation. C^{14} was not found in cholesterol of the adult cat and monkey brain after perfusion of this organ with 1-C^{14}-sodium acetate by the Geiger-Magnes technique.[5] Recent work by Davison[6, 7] with C^{14}-labeled cholesterol injected into young animals has indicated that cholesterol which enters the brain retains its C^{14} for long periods. All of these *in vivo* experiments have been supported by work with adult brain tissue *in vitro*. 1-C^{14}-sodium acetate incubated with adult rat brain slices gave cholesterol containing no C^{14} whereas other tissues tested, including newborn rat brain tissue, produced C^{14}-labeled cholesterol.[8] From at least one published experiment it appears that adult human brain tissue is as refractory as adult rat brain in its capacity to synthesize cholesterol *in vitro*.[9]

The sum of these observations has led to the conclusion that in the adult brain, cholesterol undergoes little or no turnover. It seems of fundamental interest and perhaps of future practical importance to investigate why this sterol pool behaves in this manner.

Cholesterol metabolism in the central nervous system has been reviewed, with particular reference to the somewhat unique behavior of this substance in the adult organ. Data have been presented indicating that adult rat brain tissue can perform cholesterol biosynthesis *in vitro*. These data have been used to support the hypothesis that there is a "block" in the metabolism of the sterol in the adult, intact organ and that this block is at the catabolic rather than the synthetic level.

A new approach to this problem developed when it was found that 2-C^{14}-sodium acetate injected directly into the brain (intracerebrally) is incorporated markedly into central nervous system cholesterol in contrast to result obtained when acetate is administered to brain tissue by other methods.[10] The phenomenon has been studied in some detail and occurs in the absence of the liver and viscera.[11] Later another group reported that C^{14}-labeled pyruvate and 1-C^{14}-sodium acetate are incorporated into adult brain when injected intracisternally.[12] 2-C^{14}-mevalonic acid given intracerebrally to adult rats is incorporated astonishingly well into adult brain cholesterol, and squalene turnover can be demonstrated readily following injection of this substrate.[13] In all of these experiments it was shown that although active synthesis occurred within the intact organ, the labeled cholesterol so-obtained remained labeled for an indefinite period. It has been observed in our laboratory that following the intracerebral injection of 2-C^{14}-

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* Cholesterol of adipose tissue seems to be metabolically inert like adult brain cholesterol.[1]

sodium acetate into adult rats (and cats*), cholesterol in all parts of the central nervous system remain labeled for as much as a year.[11]

How does one interpret these observations? On the one hand, cholesterol synthesis can be demonstrated in adult brain, yet the cholesterol so-obtained subsequently undergoes no turnover.** It has been suggested in a recent review[14] that "all these experiments are in agreement and amplify the previous conclusions that cholesterol is synthesized in the central nervous system of young animals, but that synthesis occurs to a much smaller extent, if at all, in adults.† This statement, although correct, seems unimaginative and misses an important point brought forth by the recent experiments demonstrating cholesterol biosynthesis on intracerebral injection of several substrates. Certainly the prolonged retention of C^{14}-cholesterol in these experiments substantiates earlier information which indicated that cholesterol in the adult brain is inert. However, if synthesis *can* occur in the adult under the conditions established by intracerebral injection, then it is implicit that the synthetic capacity is inherent in the tissue but is *held in check* under normal circumstances. Thus a new facet has been added to the problem. Where before the cholesterol-metabolizing capacity was considered absent, possibly because of the lack of proper enzymes,[16] the inertness of adult brain cholesterol may now be considered due to restraining factors: cholesterol metabolism is "blocked." From a wide variety of experiments it has been concluded that the blood-brain barrier plays a significant role in the over-all metabolism of cholesterol in the central nervous system.[17] It has also been suggested that in the normal, intact central nervous system there is a "block" in cholesterol metabolism and that this block is essentially at the catabolic rather than the synthetic level. According to this hypothesis the capacity for synthesizing cholesterol exists in the adult brain and actual turnover might occur were the catabolic stage of the latter process not blocked. Since this is at present only a working hypothesis it would be of little value to discuss whether this catabolic block may be biochemical, anatomical (a function of the blood-brain barrier) or both.

Mitigating against this hypothesis is the observation that C^{14}-labeled sodium acetate is incorporated poorly, if at all, into adult brain tissue cholesterol *in vitro*.[8] The incorporation of 2-C^{14}-mevalonic acid into adult brain cholesterol *in vitro* has not been reported, although cholesterol biosynthesis in 10-day old rat brain tissue has been studied with this substrate.[18] Literature on the metabolism of acetate by cerebral tissue is somewhat confusing.[19, 20, 21, 22] The results range from those of Scott and Libet[19] who reported that "acetic acid has no effect on the oxygen uptake or R.Q. and is not utilized by brain suspen-

* In cats for at least 4 months; unpublished observations.

** One must assume that in these experiments either a net increase in total cholesterol occurred or that during the brief period in which cholesterol biosynthesis was accomplished actual cholesterol turnover was in progress. The difficulty in demonstrating experimentally which condition actually holds is obvious.

† The conclusion which prompted this expression was based on several other experiments besides those dealing with the intracerebral injection of acetate, which at the time has only been published in abstract.[10, 15]

TABLE I

INCORPORATION OF 2-C^{14}-SODIUM ACETATE AND 2-C^{14}-SODIUM MEVALONATE INTO ADULT RAT ORGAN NON-SAPONIFIABLE FRACTIONS *IN VITRO:* BRAIN AND LIVER†

		Total Counts/Minute in Fraction‡			
Exp.	*Tissue*	ORIGINAL NON-SAPONIFIABLE	CRUDE SQUALENE*	CRUDE CHOLESTEROL**	*Substrate*
1.	Brain	23,860	210	800	2-C^{14}-sodium acetate
2.	Liver	9,660	1,128	2,780	
3.	Brain	23,000	9,636	2,760	2-C^{14}-sodium mevalonate
4.	Liver	209,820	54,696	11,040	

† Each experiment was performed by incubating 2 grams of tissue from 1 year old discarded breeder rats (290-340 Gms.) at 37° for 4 hours. Each vessel also contained 7 ml. phosphate buffer, pH 7.4, 20 mg. nicotinamide, 10 mg. diphosphopyridine nucleotide and 20 mg. $MgCl_2 \cdot 6H_2O$. Exps. 1 and 2:20 μc. C^{14}-sodium acetate, sp. act. 6.02 mc/mM. Exps. 3 and 4: 5 μc. C^{14}-sodium mevalonate, sp. act. 2.48 mc/mM as the dibenzylethylenediamine salt. Tissues for Exps. 1 and 2 came from the same animal, as did those for Exps. 3 and 4.

‡ All C^{14} determinations were performed with a windowless, gas-flow counter on infinitely thin samples.

* Obtained by chromatographing the non-saponifiable fraction on alumina and eluting with low boiling petroleum ether.

** Following the removal of the "squalene" fraction, this fraction was obtained by eluting the alumina with 1:1 acetone-ethyl ether.

TABLE II

INCORPORATION OF C^{14} INTO DILUTED SQUALENE AND CHOLESTEROL OF BRAIN AND LIVER FOLLOWING INCUBATION OF ADULT TISSUE WITH LABELED SUBSTRATES

		Specific Activity,† c./min./mg.		
Exp.	*Tissue*	SQUALENE*	CHOLESTEROL DIBROMIDE**	*Source of* C^{14}
1.	Brain	11	18 (22)	2-C^{14}-sodium acetate
2.	Liver	41	126 (181)	
3.	Brain	273	78 (102)	2-C^{14}-sodium mevalonate
4.	Liver	1,279	5,939 (7,080)	

† All C^{14} values were obtained with a windowless, gas-flow counter on infinitely thin samples.

* Obtained by addition of 50.0 mg. of triple-distilled shark squalene per gram of wet tissue to the crude squalene fractions of Table I, conversion to the hexahydrochloride and crystallization of the latter to constant specific activity from acetone and chloroform-benzene.

** Obtained by precipitating cholesterol as the digitonide from the crude cholesterol fractions in Table I. Free cholesterol was obtained from the digitonides and then converted to the dibromide. The values in parentheses are specific activity of the free sterol prior to conversion to the dibromide.

sions," to a considerably more detailed study in which 1-C^{14}-sodium acetate was used, and a definite lipogenesis demonstrated for adult brain tissue with this substrate.[22] With regard to acetate metabolism and the particular problem in question it is important to distinguish between lipogenesis and respiration. The amount of acetate converted by adult or even term fetal cerebral tissue[21] to CO_2 is apparently very small. Yet if one considers the data of Majno and Karnovsky[22] the amount of acetate converted to "total lipide," though smaller than that of peripheral tissue *in vitro,* is certainly not negligible. These investigators did not consider the contribution of acetate to individual lipides such as cholesterol.

Data illustrating our own approach to this problem and that of cholesterol biosynthesis are shown in Table I. It will be seen that both 2-C^{14}-sodium acetate and 2-C^{14}-mevalonic acid are metabolized by adult brain to non-saponifiable material, and this by minced tissue which probably does not represent the most ideal tissue preparation for this organ.* However, a large proportion of the counts in the non-saponifiable fraction produced by acetate is lost on chromatography on alumina, and so these data lose some significance; only relatively few counts were subsequently found in either the crude "squalene" or cholesterol fractions. Data on the conversion of mevalonic acid to squalene and cholesterol by brain tissues are much more significant *(Tables I and II)* because this isoprenoid substance is a direct precursor of cholesterol and is not subject to the multiple metabolic pathways acetate undergoes. A definite conversion of mevalonic acid to squalene and cholesterol was demonstrated: the specific activities are considerably greater than can be accounted for by occluded blood or other possible complicating factors. (It would seem of little merit at this time to belabor the question of whether the corresponding specific activities from the experiments with labeled acetate are significant.) It has been observed in a number of similar experiments with labeled mevalonic acid that the C^{14} in the squalene fractions is greater than in the cholesterol fractions. Although the quantitative aspects of this phenomenon are rather complicated, a simple explanation is available. The squalene→cholesterol conversion following intracerebral injection of mevalonic acid into adult brain is slower than the corresponding reaction in liver,[13, 23] and this may carry over to *in vitro* experiments also.

From all standpoints the biosynthesis of squalene and cholesterol in adult liver is considerably higher than that in adult brain. Should this be sufficient reason for invalidating the figures obtained from adult brain tissue *in vitro?* We believe not. The liver seems particularly adept at synthesizing cholesterol at a high rate for distribution to the systemic circulation. Comparison of the brain with an organ designed to actively synthesize cholesterol for extrahepatic purposes is therefore not in order. It may be criticized that the degree of synthesis of cholesterol by adult brain tissue *in vitro* does not compare with the same reaction demonstrated *in vivo* by intracerebral injection. This criticism is only weakly valid since the literature is replete with examples where brain tissue does not perform metabolic activities

* Whole brain or tissue slices gave no greater conversion to non-saponifiable material.

in vitro to the same extent it is capable of *in vivo*.[24] The present status of these experiments may reflect our inability to find the correct conditions for permitting cholesterol biosynthesis to occur properly *in vitro*. In this regard it should be recalled that at one time[25] intestinal tissue was not considered able to synthesize cholesterol *in vitro*. We now know it to be one of the most active tissues in this respect.[26]

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Carcinoma of the Liver

(Continued from page 357)

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Mankind are always happier for having been happy; so that if you make them happy now you make them happy 20 years hence, by the memory of it.—*Sydney Smith*

I do not think of truth as being made of granite, but rather as resembling a note of music, a note which we instantly recognize as the right one as soon as it is struck.—*Iris Origo*

Tumor CONFERENCE

Squamous Cell Carcinoma of the Maxillary Antrum

Edited by JOHN D. WARKENTIN, M.D.

Dr. Fink (Moderator): Today's case is one of a common tumor occurring in a rather uncommon and easily overlooked location. May we hear the patient's history, please?

Miss Gerbrandt (Senior Medical Student): The patient is a 54 year old chemist who entered the hospital on February 13, complaining of a dull pain which began in the right temporal region and radiated across his cheek. This pain had been present for six months, at first intermittently but later constantly except when relieved by aspirin. The pain had become progressively more severe until he finally sought hospitalization elsewhere about 2 months ago. There he was thoroughly examined but the cause for his facial pain was not determined. A week before his admission here, he consulted his dentist who took x-rays of his jaws and found an unerupted right upper third molar tooth. The patient insisted that this tooth be extracted. Following extraction the dentist noted a "cyst" and another fragment of tissue which he submitted to a pathologist. The pathologist's opinion was that this tissue was probably a squamous cell carcinoma. The patient was subsequently referred here for further investigation and treatment.

Past illnesses are limited to ulcer symptoms, consisting of epigastric pain relieved by food, which had been present for some 15 years. About 15 months ago the patient had an episode of hematemesis and melena, and received five units of whole blood. About 2 months before admission there was a second episode of melena, but this subsided spontaneously. A gastric ulcer was demonstrated radiographically during the previous hospitalization and the patient was started on medical treatment which he has apparently not followed too closely.

The review of symptoms was negative apart from complaints of anorexia, easy fatigability, and a 15 lb. weight loss over the past 6 months.

On physical examination, the vital signs were within normal limits. The eyes and ears were normal, but the nose showed mucosal congestion with a mucoid discharge. Examination of the oral cavity disclosed an absence of the third upper and lower molar teeth bilaterally and a decrease in the size of the right maxillary tuberosity. Sensation in the face and mouth was normal and there was no evidence of motor weakness or paralysis. A single soft, movable lymph node, approximately 1.5 cm. in diameter, was palpable in the right supraclavicular fossa. The remainder of the physical examination was within normal limits.

Dr. Fink: May we see the x-rays please?

Dr. Hartman (Resident in Radiology): The x-rays of the sinuses disclose complete cloudiness of the right maxillary antrum compared with the sharp outline and good aeration of the left *(Figure 1)*. This cloudiness is probably due to fluid, perhaps blood. It obstructs good visualization of the walls of the antrum, but there is a suggestion of destruction of its floor and erosion of its roof. This is diagnostic evidence of a malignant tumor which has eroded into the wall of the antrum.

The dental survey discloses absence of all of the molar teeth with the exception of the left upper third molar. There is considerable alveolar absorption.

The first upper gastro-intestinal series done on February 14 discloses a large penetrating ulcer, approximately 1.5 cm. in diameter, in the lesser curvature of the stomach. There is considerable deformity of the duodenal bulb. The second barium meal, given about 3 weeks later, shows considerable healing and the ulcer crater is now only a few millimeters in diameter. This indicates that it is benign and presumably unrelated to the antral disease.

Dr. Fink: Dr. Kaye, what has been done for the patient?

Dr. Kaye (Resident in Plastic Surgery): Whenever a patient is referred to our service with a tissue diagnosis made elsewhere, it is invariably our practice to obtain the slides on which the diagnosis was made

for review and confirmation by the staff pathologist here. This was particularly important in the present case, since the pathologist who examined the original specimen had been reluctant to make the diagnosis of squamous cell carcinoma. There was also some disagreement in interpretation among the local pathologists who saw this specimen, and the diagnosis finally rendered was apical granuloma of the upper third molar tooth.

However, after the x-rays of the sinuses had demonstrated the opacity and destruction of the right maxillary antrum, it was apparent that this diagnosis might be in error and that another biopsy was imperative. This was done by the Caldwell-Luc approach through the mouth. An opening into the right maxillary antrum was made and specimens of tissue were taken from all areas. The pathologic diagnosis this time was unequivocally squamous cell carcinoma.

A second, more definitive operation was then undertaken. A direct approach to the antrum was made through an incision which split the upper lip, then curved laterally along the naso-facial crease and beneath the eye. This gave excellent exposure of the antrum. The tumor could now be seen to involve much of the maxilla, including its floor, posterior wall, roof, and the alveolar ridge. It had broken through the wall to invade the region of the pterygoid muscles. As much of the tumor as was possible was removed. The bony walls of the antrum were all removed with the exception of the floor and the orbit, since removal of the latter would have necessitated orbital exenteration. We realized that the tumor had already extended too far to be removed completely and that further treatment would be required.

Post-operatively, the patient has done well. His incision has healed with the exception of a small draining sinus. In spite of the considerable amount of tissue that was removed, there is little resultant cosmetic deformity. Inside his mouth, however, there is a small hole which goes back into the antrum and into the pterygoid muscle region behind the tuberosity of the maxilla. As a result of this, there is slight regurgitation of fluid through the nose when the patient drinks. The quality of his voice, however, has not changed appreciably. Within the past few days he has had a recurrence of his headache in the right frontotemporal region. He has been examined by a neurologist who believes that this pain is probably due to the extension of the antral carcinoma along the first and second divisions of the trigeminal nerve. Radiation treatment with the CO^{60} unit has been started.

Dr. Fink: Dr. Mantz, will you describe the surgical specimens, please?

Dr. Mantz (Pathologist): First, I will point out one aspect of the development of the tooth which may provide the pathologist with difficulty in interpreting the presence of infiltrating masses of epithelium oc-

Figure 1. View of the maxillary sinuses shows marked opacity on the right. There is evidence of destruction of the floor of the right maxillary antrum.

curring within the gingiva or the deeper tissues of the alveolar ridge. At about the 6th week of gestation, the ectoderm overlying the developing jaw undergoes localized thickening of its basal layer. This proliferating ectoderm soon invaginates to form the enamel organ which then continues to grow inward as a bell-shaped structure with the mesenchymal dental papilla filling its inner cavity. The innermost layer of cells of the enamel organ differentiates into ameloblasts whose function is, firstly, to induce the differentiation of the adjacent mesenchymal cells into odontoblasts and, secondly, to lay down the enamel of the crown. This second function, of course, is carried on only by the ameloblasts in the tip of the cusp and not be those covering the root. After the ameloblasts of the root have fulfilled their function of induction, they separate from the root, but remain within the fibrous periodontal membrane as small islets of epithelial cells known as the epithelial rests of Malassez. These rests may be found within the membrane at any age after the roots have formed and are not infrequently seen by the pathologist. During dental infections or abscess formation around the tooth, this epithelial tissue is frequently stimulated to grow, and may give rise to an epithelial lining to the abscess, resulting in a radicular cyst. In other cases, small islets of proliferated squamoid epithelial cells may be scat-

tered throughout the chronic inflammatory tissue and give the appearance of an invasive neoplasm. The pathologist confronted with a piece of such tissue has a difficult choice to make. He sees evidence of inflammation and fibrosis with scattered islets of epithelial cells. Do these islets represent a proliferative reaction of the rests of Malassez, or are they neoplastic? This is the dilemma which we faced in interpreting the tissue which the dentist originally removed from this patient after extracting his tooth.

With this background, let us now examine the slides from the original biopsy. We see considerable inflammation, fibroblastic proliferation, and many foreign body giant cells, but in addition, there are many islands of epithelial cells which are not particularly squamoid, tend more to be reticular or fusiform, and closely resemble the rests of Malassez *(Figure 2)*. It is understandable that there was some difference of opinion among reviewing pathologists. Those that felt the lesion was frankly carcinomatous had to yield on the basis of clinical evidence that was presented at that time, since extensive x-rays, not including the films you saw today, showed no evidence of destruction of bone and nothing to suggest disease within the sinus.

The gross specimens from both operations performed here consisted of irregular pieces of firm granular tan tissue, sometimes adherent to fragments of bone. The microscopic appearance of all of these fragments is similar. Instead of the usual covering of ciliated columnar respiratory epithelium, there is either ulceration or a covering of keratinized squamous epithelium. More significant, however, are the numerous islands of epithelial cells within the underlying fibrous stroma. These neoplastic epithelial islands have invaded to great depth and extensively destroyed the bony wall of the antrum *(Figure 3)*. In places the floor of the sinus is entirely gone and is replaced by the infiltrating tumor with its attendant fibroblastic reaction. The tumor also extends downward into the alveolus of the underlying jaw from which the impacted wisdom tooth was originally removed. In places there is reactive new bone formation. The majority of the tumor cells are not typically squamous but tend to be more columnar, although some do form whorls and small keratin pearls *(Figure 4)*.

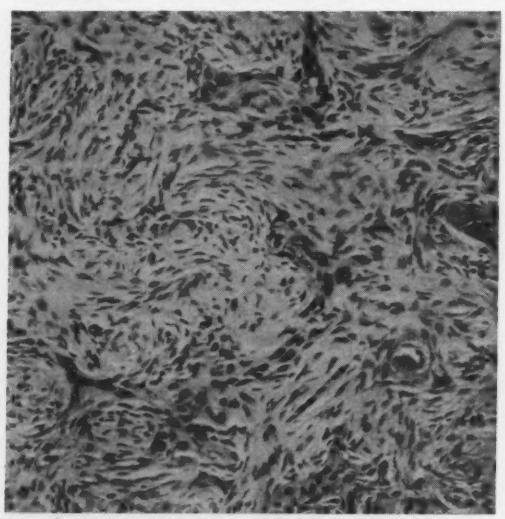

Figure 2. Photomicrograph of the original biopsy of the alveolus shows irregular nests of fusiform epithelial cells lying within proliferating fibrous tissue. Hematoxylin and eosin. ×160.

In the floor of the maxillary sinus there was a large polypoid mass which grossly might very well have been mistaken for an inflammatory polyp. Its surface is covered with the usual respiratory type epithelium but the substance of the polyp is composed of more of the same extensively infiltrating tumor.

The tumors arising from the mucosa of the nose and nasal sinuses are quite characteristic and differ from those of the posterior nasopharynx in their histogenesis and biological behavior. The boundary between the two areas is a vertical line drawn approximately through the posterior end of the middle and inferior turbinate bones. Epithelial tumors occurring posterior to this line tend to be anaplastic, and include the so-called lympho-epitheliomas. Those originating anterior to this boundary, such as the tumor presented today, arise from the so-called Schneiderian membrane and usually are well differentiated carcinomas of either squamous or mucoid variety. A third group of tumors originates from the mucous glands; these closely resemble those arising in the major salivary glands. The mucous membranes of the nasal sinuses have an amazing propensity for giving rise to squamous cell carcinoma. This is particularly true in the maxillary sinus and especially in the mucosa which covers its floor. Those tumors arising from the roof and lateral walls of the antrum tend more often to be polypoid mucus-secreting adenocarcinomas. The characteristic behavior of these so-called Schneiderian carcinomas, whether they be squamous or adenocarcinomas, is local infiltration and destruction rather than widespread metastasis. They metastasize very late if at all. The tumors arising in the floor of the antrum frequently invade downward into the alveolar sockets so that the dentist is often the first to see such a patient because of a loose tooth. Following extraction, he will note a small amount of abnormal tissue and if he submits this for histologic examination, the diagnosis may be made.

Dr. Fink: Dr. Robinson, may we have your comments?

Dr. Robinson (Surgeon): Dr. Mantz has mentioned the excellent opportunity that dentists fre-

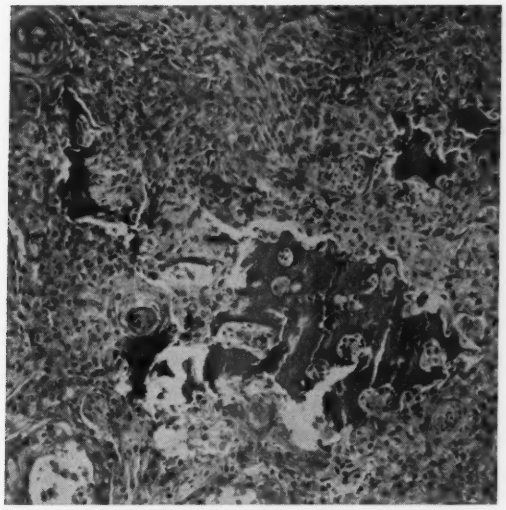

Figure 3. Photomicrograph of the wall of the antrum illustrates the extensive destruction of bone by tumor invasion. Hematoxylin and eosin. ×100.

quently have for discovering tumors of the jaws and maxillary antrum. Unfortunately this opportunity is not always taken advantage of. It is difficult to ignore extrusion of tumor tissue from a socket after a tooth extraction but sometimes this happens. It is also of importance to pay close attention to the healing of the wound after tooth extraction. Whenever such a wound does not heal promptly, the dentist or physician should become strongly suspicious. Patients with non-healing holes after dental extraction are still too frequently being followed for 2 or 3 months before adequate investigation, thus delaying the diagnosis of a cancer. In today's example, the dentist who extracted the tooth is to be commended for his high degree of suspicion and prompt action.

A second lesson this case illustrates is the importance of taking an adequate biopsy and if necessary, repeating it again and again. When a pathologist is uncertain of the diagnosis or when disagreement exists among two or more pathologists, the responsibility for pursuing the problem remains with the clinician. If the clinician is strongly suspicious that a given lesion is malignant but receives a negative report from the pathologist, he should take another biopsy, and if necessary another, until he is satisfied about the tissue diagnosis. We, as clinicians, must remember that any biopsy will show the pathologist only the limited picture of the particular piece of tissue that was removed, which may not be representative of the entire lesion. If the biopsy is too small or is removed from the wrong place, the pathologist cannot give the correct interpretation of the tissue that has been left behind. Sometimes we also err in supplying the pathologist with insufficient clinical information, so that again his interpretation is one-sided and must be based entirely on the histologic appearance.

Carcinomas arising in the superior alveolus may present around the teeth or they may grow up and erode into the antrum. Once they have eroded into the antrum, it may be impossible to say whether they originated in the antrum or in the alveolus. These tumors may not give rise to symptoms until considerable destruction of bone has taken place and so, may, of course, be inoperable when first discovered. The treatment of tumors of the antrum or alveolus is surgical removal whenever possible. However, once they have involved the bone, they may be extremely difficult to eradicate by operative means. In such cases, we follow the operation with radiotherapy. This approach is illustrated in today's case in which the tumor had extended up into the base of the skull, and there was no possibility for a complete surgical extirpation. I deplore the practice of simply making

(Continued on page 370)

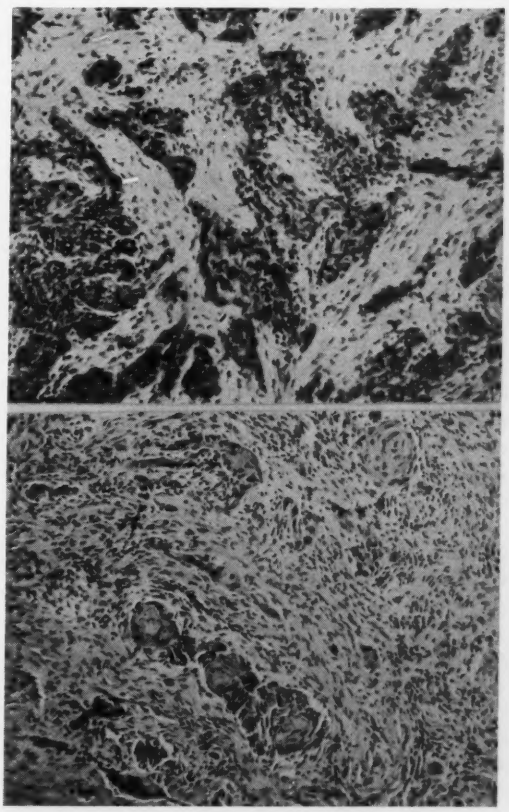

Figure 4. Photomicrograph of the tumor. Hematoxylin and eosin. ×100. (Top) The tumor cells are disposed in patternless clusters. The majority are columnar or fusiform. (Bottom) Cellular whorls and small keratin pearls also occur.

Struma Ovarii: Its Concept

CHARLES R. BROMAN, M.D., ***Galveston, Texas***

TO THE PRESENT there have been about 250 cases of struma ovarii (or objects so designated as struma ovarii by the authors) described in the literature. Those cases, up to 1946, have been exhaustively documented and analyzed by Smith. Since his article there have been at least 80 additional cases recorded for the most part situations in which an ovarian thyroid is associated with unusual circumstances or has resulted in unusual manifestations. Organization of these data is clearly indicated; however, to tabulate this would seem to me to be a most exacting and disagreeable task of organizing cold statistics. On the other hand, it would be interesting, albeit not essential, to probe into the background surrounding the development of the struma ovarii concept. To this aim this paper is directed.

The most recent publication giving the results of 69 years of speculation, observation and rumination concerning struma ovarii presents a clear current concept of this rare entity:

Thyroid tissue, which is a frequent constituent of teratoma, may overgrow all other elements, producing tumors made up entirely or in large part of thyroid tissue. This, at any rate, is the generally accepted explanation of such tumors, which, however, are rather rare.

While the histologic picture in the typical case leaves little doubt as to the thyroid nature of the tumor tissue, one may be misled by the pseudothyroid appearance at times seen as a result of degenerative changes in either adenocarcinoma or cystadenoma of the ovary. That genuine thyroid tissue is concerned, however, has been demonstrated by chemical determinations of the iodine content as well as by biologic tests with the tumor tissue. As a matter of fact, there is a small group of cases in which the thyroid tumor of the ovary was apparently functionally active, producing clinical evidences of hyperthyroidism. While such tumors have seemed relatively benign in most cases, in a number of reported instances they have run a definitely malignant course, with metastasis and death. The mere presence of a small amount of thyroid tissue would not justify the designation of ovarian struma. It must make up a dominating area of the tumor, although no hard and fast rules can be given. Furthermore, only a fraction of tumors of this group are associated clinically with hyperthyroidism, and in these there is evidence of the same sort of hyperplastic change which characterizes the overactive thyroid gland.

Arrival at this milestone has been via the work of many investigators. It has involved not only an understanding of the thyroid tumor but also of dermoids and teratomas, with which it is so intimately related. Wilms, as long ago as 1895, showed that the term dermoid, as usually applied to ovarian cysts, was a misnomer. It had arisen from an erroneous conception of their structure, then generally

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This is one of a group of theses written by fourth year students at the University of Kansas School of Medicine, selected for publication by the Editorial Board from a group judged to be best by the faculty at the school. Dr. Charles R. Broman is now serving internship at the University of Texas Medical Branch, Galveston, Texas.

considered to be a simple ectodermal formation. At that time, on the ground that all ovarian dermoids contain the three germinal layers, he advanced the dictum that there exist in the ovary no tumors composed only of skin. It was his opinion that the cystic type of dermoid should be termed embryoma and the solid type teratoblastoma. Somewhat later Pfannenstiel, who accepted Wilms' conclusions, made the additional point that ovarian dermoids or cystic tumors differ from ovarian teratomata or solid tumors chiefly because dermoids exhibit elements partially or completely recalling fetal or adult organs of the human body, and so are benign. Teratomas, on the other hand, exhibit elements of the three germ layers growing with unrestrained licence and exhibiting a cell structure atypical in form, size and arrangement, and so are malignant.

These early observations have stood the test of time so that today teratoma and dermoid cyst are considered together, the latter constituting only one variety, though by far the most frequent, of the former. The histogenesis of the two is identical, though they present certain important points of difference as to gross microscopic characteristics and clinical course. Authors differ somewhat as to the basis of distinction between the two but the following generalizations can be drawn:

1. The dermoid is a cystic tumor, the teratoma a solid one, though it may show occasional small cystic areas.

2. The dermoid is characterized by a predominance of ectodermal elements, though mesodermal elements and occasional entodermal structures are also found. The teratoma always shows a conglomeration of elements derived from all three germinal layers. It is fact, however, that no sharp dividing line can be drawn on this basis.

3. The dermoid cyst is a benign tumor, all the abnormal tissue elements being well differentiated. The teratoma is to be classed as a malignant one, the fetal elements being of undifferentiated type, and the clinical course being characterized by such malignant features as recurrence and metastasis with death. It is this third criterion which one author declares to be the most important.

Before continuing, a word in regard to nomenclature of these ovarian thyroid tumors is in order. Various terms have been applied to them by the different authors, some rivaling in length and complexity the names of organic chemical compounds. They were originally described as "struma thyreoidea aberrata ovarii" but in quick succession several other names were suggested—"struma ovarii colloides," "teratoma strumosum thyroidiale ovarii," "Struma ovarii." Another writer offered as the perfect compromise "teratoma thyroidiale ovarii." Although it gives neither origin nor anatomy, however, the title which has emerged as the most popular, hence acceptable, is "struma ovarii." It was first used by Meyer in 1903 and gained almost immediate acceptance by American authors even though their German colleagues were somewhat more reluctant. More than likely the term's quick acceptance was due more to its brevity than any other single factor.

It is commonly considered that the first of these growths to be described in the literature was recorded by Boettlin in 1889. He wrote of a small group of vesicles "showing almost complete histological agreement with the parenchyma of the thyroid" in an ordinary, typical ovarian dermoid (with skin, hairs, etc.). His short accompanying description is clear enough but Boettlin did not show with sections and stains that the "colloid vesicles" are simply not tubular mucous glands distended with their inspissated secretion.

The next mention of ovarian thyroid tissue was by Wilms in 1895 in his curious ovarian "embryo" with the endoderm on the "dorsal" surface of the "brain." He mentions a respiratory type canal partly surrounded by "a well developed thyroid undergoing colloid degeneration," and adds that "I can save myself a description of the latter, since the appearances are so typical that a mistake is excluded." Wilms again (1896) says of a solid teratoma with thyroid, that "between the cysts there lies a well developed organ, the resemblance of which to a thyroid cannot be mistaken. The partly formed vesicles are filled with colloid as in that gland." There is no evidence in either case apart from personal opinion that we are not concerned with "resemblance."

Merttens in 1897 in a paper dealing chiefly with dermoid teeth mentions "glandular vesicles in large numbers, resembling those of the thyroid." Unfortunately the accompanying figure is only a rough diagram with no histological details.

Kroemer (1899) enjoys the distinction of being the first to combine both description and drawing in such a manner that those who cannot see his specimen are satisfied. The object, a typical ovarian dermoid, contains a canal of respiratory type and, at one spot close by, a gland the size of a pea, that "reveals itself under the microscope as normal thyroid. . . . The gland, supplied with nerves and vessels, lies in a capsule of its own. The follicles present only slight differences in volume, are lined with low epithelium and filled throughout with tough colloid. Hardly anything of stroma is present." The excellent drawing amply confirms Kroemer's statements.

Next, Katsurada in 1901, said that two of his ovarian dermoids contained thyroid. In the first "one sees in the immediate vicinity of an island of cartilage a fairly well developed but irregularly

formed thyroid. The tubules of the gland are lined with a simple layer of cubical epithelial cells, and a few contain colloid substance." In the second dermoid "the presence of thyroid tissue, more correctly, of a high degree of struma colloides in the cyst-wall is of great interest. Formation of colloid and extent of vesicles are generally very extensive; several of the latter form larger cysts containing brownish or dark brown masses of colloid. In this thyroid one finds every here and there a small number of follicle-like aggregates." Had Karsurada augmented his sketchy descriptions with legible figures, he would presumably have established the second case as a genuine ovarian thyroid.

For reasons not quite clear the above seven cases are only rarely mentioned in the literature. There are, however, two additional cases which cannot be lightly passed over, for they are the foundation on which controversy was established. To the seven cases, therefore, must be added the first example of pure ovarian goiter described (1899) and accepted by almost all authorities. It was not, curiously enough, accepted by Gottschalk, the author himself. Gottschalk was convinced that his tumor was a "folliculoma malignum ovarii" as explained by him:

A firm brownish red tumor of the left ovary of a forty-eight year old para three; 10 x 8 x 3.5 centimeters, the periphery with large cysts, the center honeycombed with minute cysts, all with colloid contents. A capsule is present but ruptured in places. "At first sight the picture is reminiscent of struma maligna," i.e., solid 'syncytia' and closed 'syncytial' vesicles with daughter vesicles at their periphery. "There can be no doubt that we are dealing with a neoplasm of anatomical and clinical malignancy which has arisen from the wall of primordial follicles."

Evidently Gottschalk thought the tumor malignant for the sole apparent reason that ovarian follicles are confined to the cortex but the whole medulla was occupied by vesicles in the specimen. This stand was taken in spite of the fact that the woman was in continued good health a year after the operation. Gottschalk's beautiful illustrations show typical thyroid, somewhat immature and cellular in places, adult in others with plenty of colloid vesicles, a few abnormally large but without a solitary objective indication of malignancy. In all communications Gottschalk referred to his tumor as "similar to struma malignum." This is certainly not a phrase one would use to convey the idea that it contained thyroid tissue; the term struma malignum does not convey a correct idea of the pathologic anatomy presented by an ovarian tumor of this type.

The second aforementioned case, a similar specimen, was studied and described by Kretschmar two years later (1901). The first report of his case was read before the Gynecological Congress at Giessen. At that time Kretschmar made no reference to thyroid tissue observed in his tumor and his statements show he did not suspect any. Kretschmar interpreted his case as an endothelioma, since he thought he could demonstrate the occurrence of the primary tumor elements always within preformed lymph spaces, a proliferation of whose lining endothelium he believed to be the causative factor. If, indeed, Kretschmar's tumor were to be classed as an endothelioma, it would be an endothelioma of adenomatous type. At a glance an adenomatous endothelioma looks like thyroid tissue but on careful examination of serial sections it is seen that every vesicle in the endothelioma has a canal in its center, which is not the case in thyroid tissue. In addition, every section of an endothelioma shows lymph tubules with open canals and nothing similar is seen in thyroid tissue.

When Kretschmar reported his case, no ovarian thyroid tumor had been recognized which contained other tissue such as hair, salivary gland or bone. He was led to believe, therefore, that the thyroid tissue in an ovary was a metastatic deposit from the normal or abnormal thyroid gland. He based his opinions upon the reports of Riedel and of Oderfeld and Steinhaus who found metastatic deposits in the jaw and frontal bone originating from apparently normal thyroid glands.

So much for the evidence available in 1902—one established nodule of thyroid in a dermoid (Kroemer) and two misinterpreted ovarian goiters without demonstrated admixture of other tissue (Gottschalk and Kretschmar). This would not appear to be sufficient evidence on which to build any sort of theory. However, in 1902, Ludwig Pick gained the distinction of being the first to clearly describe and properly classify these ovarian thyroid tumors or, as he termed them, "struma thyreoidea ovarii aberrata." In another paper, he pointed out that Gottschalk's "folliculoma malignum ovarii" and Kretschmar's "endothelioma" were actually perfect examples of thyroid tumors of the ovary. Pick's description of the best specimen in his series, as transcribed by Dingels, runs thus:

"The tumor is a small-man's-fist-sized cyst" (an ordinary ovarian dermoid with skin, hair, teeth, etc.). "In immediate contact with a bay-like invagination" of the cyst wall "there is a largish body, 3 x 3 x 1 cm., of partly brownish, finely porous consistence, of partly more coarsely cystic structure; one finds a large number of miliary, lentil-to-pea-sized cysts with tough transparent, partly yellow, partly greenish, partly brown contents. . . . There is no doubt that we are dealing here with nothing else than a thyroid gland presenting the picture of so-called colloid struma. The microscopical picture teaches this conclusively;

and the positional relations of the body to the rest of the 'anlage' agree. The skin with hairs corresponds to the scalp, the shallow bay with the teeth at its borders to the oral cavity, and exactly corresponding with thyroid does the flat stratified epithelium of the oral bay change suddenly and quite abruptly to stratified ciliated epithelium, agreeing exactly with the normal neighborhood of the respiratory tract and thyroid."

A glance at Pick's two original illustrations showing undoubted thyroid vesicles and liquefying thyroid stroma will convince those who doubt his description.

Shortly thereafter, Pick, in an extended discussion with Gottschalk before the Berlin Medical Society, advanced the theory which is now accepted, that these thyroid-like tumors of the ovary whether or not they contain derivatives of other embryonic tissues, are in fact teratomata. The entodermal elements of the thyroid anlage have undergone excessive development, with a consequent partial or complete suppression of all other tissues. This startling new theory, as far as can be determined, was based on the following observations:

1. Pick states he "found these structures" (thyroid tissue in dermoids), "previously regarded as rarities, in six of his latest twenty-one examined cases, often only sparingly, but regularly presenting the picture of struma colloides, partly with formation of large cysts."

2. Pick cites the celebrated case reported by Saxter, in which a single, well-formed tooth was found in an otherwise healthy ovary. This occurrence he believes to be explainable only on the theory that a teratoma had started to develop but that all other tissues than those of the tooth had for some reason undergone atrophy and eventual disappearance.

3. Pick also observed that often, along with the thyroid tissue, there was also found in these ovaries a variety of other structures such as bone, teeth, hair, cartilage, and nervous tissue. Calcium, cartilage and even bone may appear in degenerating thyroid tissue. But degenerative changes cannot account for the presence of the hair, teeth, etc. in these tumors. The variability in association of these structures suggested an embryonic displacement into the ovary of multipotent cells which might proliferate in the direction of any type of tissue.

4. Pick drew attention to the fact that metastases from the thyroid gland almost always are located in the bony skeleton. To suppose that thyroid metastases are found solely in ovaries requires undue stretch of the imagination.

In a later writer's opinion, however, the strongest argument is to be found in the fact that a considerable number of tumors have been reported showing various intermediate stages between the two end types—a large cystic teratoma with an almost insignificant area of thyroid tissue on the one hand and a good sized tumor consisting purely of this on the other. These types may be considered as forming the extremities of an unbroken series, throughout which the thyroid tissue shows varying degrees of development, having in a few instances completely suppressed all other elements. Of especial interest and significance in this connection are the painstaking investigations of Walthard, who undertook the extensive labor of making complete serial sections of three such ovarian tumors.

After the appearance of Pick's article, Gottschalk wrote another paper on the subject, contradicting himself a number of times. In his later communication he refuted Pick's diagnosis and declared his original one "folliculum malignum ovarii" correct. He further stated that his tumor developed from the wall of a primative follicle and showed a strong similarity to so-called folliculum. Because he found the smallest locules in the periphery of his tumor, Gottschalk concluded it developed from the periphery of the ovary, disregarding the fact that the same formation is observed in all cystic tumors.

Kretschmar, who had originally diagnosed his tumor as an endothelioma, was struck by its similarity to thyroid tissue upon reexamining it after the appearance of Pick's paper but was unable to bring himself to the atypically-developed teratoma theory. Although giving up the endothelioma diagnosis and admitting the identity of the tumor tissue with that of the thyroid, he continued to explain the presence of this tissue in the ovaries on the ground of a metastasis from the thyroid gland. The chief stumbling block in the way of this interpretation was the fact that some small areas of bone were present, a circumstance that, as Kretschmar admitted, strongly strengthened the teratomatous theory of origin. He believed, however, that they may have merely represented the end-result of metaplastic changes in the connective tissue, the same thing being found in the so-called ossifying strumas of the thyroid gland itself.

Another author who was unable to accept the teratoma theory, or indeed to believe that the thyroid-like tissue occurring in ovarian tumors had anything to do with the thyroid whatever, was Bell. He described two large, multilocular cysts, each containing a small area of tissue which he admitted showed practically histologic identity with that of the thyroid. He believed, however, that this was in reality merely the result of a peculiar colloid degeneration of an ordinary cystadenoma of the ovary, the epithelial lining of the acini having been flattened out by pressure. He stated that he had seen a very similar histologic picture produced in a kidney by complete obliteration of the ureter.

With these exceptions the majority of authors who

discussed these questions have more or less accepted Pick's theory. Subsequent to these earlier efforts, the identity of the thyroid tissue has since been indisputably proven—morphologically, pharmacologically, chemically and biologically—by Plaut in 1933. Although it is difficult to establish definite criteria as to the characteristics necessary to classify a teratoma among the strumas of the ovary, it seems necessary in order to exclude tiny nodules of thyroid in dermoids from this rather specific group. Accordingly, one group feels that a tumor should fulfill at least one of the following criteria to justify its position:

1. Thyroid tissue composing at least fifty per cent of the solid mass of the ovarian tumor.

2. Evidence of physiologic overactivity of struma ovarii in the form of clinical hyperthyroidism with subsequent regression after removal of the ovarian tumor.

3. Major pathologic changes in the ovarian thyroid, other than that seen with overproduction of the hormone.

This is the concept of struma ovarii which is held to be true in this, the middle of the twentieth century.

Editor's Note: References may be obtained by writing the JOURNAL OF THE KANSAS MEDICAL SOCIETY, 315 West 4th Street, Topeka, Kansas.

New Drug Firm

The recent June American Medical Association Meeting in New York served as a launching pad for a new drug manufacturing enterprise—Philips Roxane, Inc.

Philips Roxane rises out of a vast network of technological operations here and abroad from which its extensive plans for pharmaceutical research and development have been drawn. In the background are a number of corporate operations. Among these are the Philips Electronics and Pharmaceutical Industries Corp. and N. V. Philips-Duphar of The Netherlands.

To enhance and facilitate its research and marketing operations in this country, Philips Roxane has acquired several American affiliates. Among these is the Columbus Pharmacal Company of Columbus, Ohio, which henceforth will operate under the new Philips Roxane name.

Another affiliate has been acquired at the location of the headquarters for Philips Roxane in St. Joseph, Missouri—the Anchor Serum Company of that city.

The product scope of Philips Roxane was further extended with the acquisition of Thompson-Hayward Chemical Company, of Kansas City, Missouri.

The unusual institutional character of the initial promotional step taken by Philips Roxane at the American Medical Association Meeting was in keeping with its non-commercial approach in introducing itself to the medical profession.

Tumor Conference

(Continued from page 365)

a hole in the wall of the antrum and putting in radium. This is not enough. Surgical extirpation followed by radiation is much more effective.

The prognosis depends on the degree of direct extension. If the tumor is still localized, there is a reasonably good chance of salvage of about 30 to 40 per cent of cases, but once it has spread widely through the antrum, particularly posteriorly into the pterygoid region, the survival rate is very low.

Dr. Fink: Dr. Tice, do you have any comments about the radiotherapy of these tumors?

Dr. Tice (Radiologist): In 1949, I reviewed the cases of cancer of the antrum that had been treated at the Kansas University Medical Center.[1] My main interest was in those that had been treated with radiotherapy supplementing some form of surgical treatment. There were 57 such cases, of which 47 were considered primary in the antrum. This series included all malignant tumors, carcinomas and sarcomas, of which 21 were primary squamous cell carcinomas. Our treatment of these cases consisted of intra-cavitary radium insertion sometimes followed by external radiation in varying doses. We achieved a 27 per cent five year survival in the group with primary tumors. This is lower than the majority of reports on this group of tumors. Cases that come to the radiologist for treatment, however, are usually already far advanced, as illustrated by these patients; 80 per cent already showed evidence of bone destruction. We had no early case in our series.

As I have observed these tumors handled over the years, I have become convinced that our best results are obtained by a conservative surgical procedure to open into the antrum followed by radiation therapy. As much tumor as possible is cleaned out of the antrum through this opening, and a pathologic diagnosis is obtained. This is not a radical procedure. The radiologist should now take over. A radium source, either needles or a capsule, is implanted in the antrum for a predetermined dose. Following this, external radiation should be given. In our institution, this was previously accomplished with 250 KVP (Ortho voltage) therapy. We now use CO^{60}. We try to get a total intra-cavity and external dose of 10,000 gamma roentgens or more. We have been gratified by the large dose that can be applied with little or no necrosis.

Reference

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The President's Message

DEAR DOCTOR:

One has only to look over the program of matters discussed at the recent American Medical Association meeting in New York by its House of Delegates to realize how very important all of this is to the practice of medicine in the United States by both ethical and unethical physicians; the latter are subject to discipline which it is hoped will change their methods. Many of us have had experience and know how easy it is to assume a critical attitude toward one's competitor, but usually it seems very difficult for doctors to take definite punitive steps against the rare and occasional M.D. who is really guilty of drastic violation of medical ethics such as grossly over-charging, charging one fee when the patient has no insurance and a much higher fee to the one who has insurance. There are also the few doing unnecessary surgery, as well as fee splitters and rebaters. We have the machinery to deal with these and other faults in a very few M.D.'s in the Grievance Committee of our county Medical Societies. It seems difficult to get doctors to use it. Not many physicians are guilty, but let's see that those who are receive punishment.

Many states have been plagued by the osteopathic controversy. Thank goodness, ours is apparently being ironed out satisfactorily in Kansas, and California has taken a tremendous step forward in the troubled condition there. It looks very much to me as though the whole problem has been pretty well solved in the past two years by action at all three levels of our Medical Societies.

Let's all boost for organized medicine and help make it work.

Fraternally yours,

Harold M. Glover, M.D.

President

The Kansas Press Looks at Medicine

Editor's Note. In this section the JOURNAL reproduces editorials relating to medicine which have appeared in the lay press. An effort is made to include both favorable and unfavorable comments, and the Editorial Board in no instance assumes responsibility for the opinions expressed.

(This clipping is not from Kansas but is of such particular interest, especially to the young men and women studying medicine that the Editorial Board requested and received permission from the *Omaha World-Herald* for its use here.)

DOCTORS AND "SOCIETY"

"The practice of medicine is a public trust," Secretary of Health, Education and Welfare Abraham Ribicoff told the graduating class of the University of California Medical Center this week.

Has any young man or woman on the threshold of a medical career thought otherwise?

"Each of you in your two decades of training thus far has been heavily endowed by the people of your community, your state and country," Mr. Ribicoff continued.

Has any fledgling physician ever disputed that fact?

"Nor will the public interest in you end when your education is completed . . ." the Secretary said. "Public laws will govern your practice. The hospital in which you work will be licensed by the public, and may well have been built or equipped with public funds."

Those statements are elemental, as every graduating doctor in the land knows full well. But then Mr. Ribicoff turned to the realm of forecast. He said:

"In a few years you will come into your own as full-fledged practicing physicians. The new world that is yours to serve will be very different from the world as it was when you began your long preparations. . . . The very texture of our society will be different."

What did the Secretary of Health, Education and Welfare mean by that? Did he mean that doctors of the future will have to adjust themselves to the Big Brother "texture of society"? Did he mean that because the public has taken a deep interest in the education of its doctors and has supplied some funds to build hospitals, medical graduates should feel obligated to consider themselves servants of the state, and beholden to some socialistic bureaucracy in Washington?

If that's what Mr. Ribicoff meant, we hope, with a considerable degree of confidence, that every young man and woman, now and in the future, who has the savvy to earn a degree in medicine will also have the courage to say to him nay.—*Omaha World-Herald,* June 7, 1961.

HORSE-AND-BUGGY SYSTEM

The present squabble involving the county coroner's office is simply further evidence that the coroner system is inadequate for 20th Century requirements.

The coroner is both a medical and a legal officer. He logically should be qualified in both medicine and law. But no such qualifications exist in the Kansas coroner system. Any citizen is eligible to run for the job, whether he knows anything about it or not.

Another defect of the system is that the coroner's office is not coordinated with other county offices. As a result, conflicts like the present one often crop up, and their effect is to hinder the detection and prosecution of crime.

The solution to the problem has long been before us. The medical examiner system, under which autopsies and inquests would be performed by professionally qualified persons, would be free of the obvious defects which now exist.

To replace coroners with medical examiners would

(Continued on page 376)

From the Stacks

State Medical Library

MRS. BLENDENA EVANS, *Librarian*
Stormont Medical Library, State House
Room 516, Topeka, Kansas
Phone CE 5-0011, ex. 297

Monographs available in the library.

Marriage Manuals

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Books and periodicals will be sent anywhere in the state. You pay only the postage, four cents for the first pound and one cent for each additional pound.

Physiology

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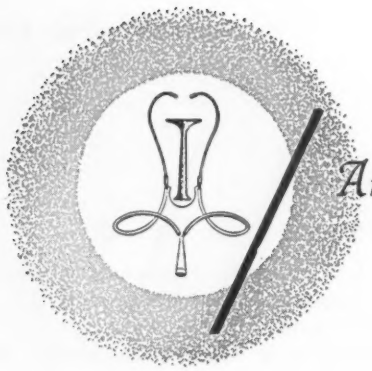

Announcements

Professional meetings, conferences, and postgraduate courses of national importance are listed for the **Doctor's Calendar.** ***Notice of the session is posted in advance to allow the physician time to make preparations.***

A personnel exchange agreement in medical education between the School of Medicine of the University of Kansas and the College of Medicine of the University of the Philippines will begin this fall. Dr. C. Arden Miller, dean of the school, announced that funds to support the program for its first year (September, 1961 through December, 1962) have been granted by the China Medical Board of New York, Inc.

The exchange will involve undergraduate medical students, graduate students in the basic science departments, resident physicians in clinical training and faculty members at all levels. During the first year, two students from each classification and two faculty members will be exchanged to each University. Periods of exchange will range from three months to a year for students. At the faculty level, it is anticipated that the period of exchange would not be less than nine months for junior staff members and no shorter than two months for senior members. Visiting faculty members in either institution will serve actively in all programs of the departments to which they are attached.

The Thirteenth Postgraduate Assembly in Endocrinology and Metabolism, under the Co-Sponsorship of The Endocrine Society and the National Institutes of Health, will be held in Bethesda, Maryland, on October 2-6, 1961. A comprehensive review of clinical endocrine problems and current research activity in these areas will be presented. For further information, write to: Dr. Roy Hertz, National Institutes of Health, Building 10, Bethesda 14, Maryland. The fee will be $100.00 for physicians, with a reduction to $30.00 for Residents and Fellows. Enrollment limited to 100.

The Department of Otolaryngology, University of Illinois College of Medicine, will conduct a postgraduate course in Laryngology and Bronchoesophagology from October 23 through November 4, 1961, under the direction of Paul H. Holinger, M.D.

Registration will be limited to fifteen physicians who will receive instruction by means of animal demonstrations and practice in bronchoscopy and esophagoscopy, diagnostic and surgical clinics, as well as didactic lectures.

Interested registrants will please write directly to the Department of Otolaryngology, University of Illinois College of Medicine, 1853 West Polk Street, Chicago 12, Illinois.

A postgraduate course in Pediatrics, Clinical and Research Advances in Pediatrics and Child Guidance, will be presented by The University of Colorado School of Medicine in Estes Park, Colorado, at The Stanley Hotel on August 21-25, 1961. Further information may be obtained from the University of Colorado Medical Center, Office of Postgraduate Medical Education, 4200 East Ninth Avenue, Denver 20, Colorado.

USE YOUR MEDICAL LIBRARIES

YOUR LIBRARIAN WILL BE HAPPY TO ASSIST YOU

Two-Way Communication With Members

Kansas Blue Shield Participating Physicians often have questions about the relationship of members with the Plans. These are fair questions and are increasingly significant in view of today's criticism of prepaid health care programs. They ask:

- What is Blue Cross-Blue Shield doing to let members know about their benefits?
- Is there a way to better inform them of policy changes?
- How effectively are problems of prepaid health care being explained to members?

The Blue Cross-Blue Shield Education Division in its role of communicating with members, has the responsibility in a large part for answering these questions.

Publications, ranging from inserts in billing notices, and *Health Plan,* the Blue Cross-Blue Shield quarterly publication, to expanded newspaper and television advertising, give members the details of benefit changes, current trends in health care economics, and suggestions concerning the upgrading of coverage.

However, perhaps the one most significant educational activity sponsored by Blue Cross-Blue Shield in Kansas is the program of "grass roots" meetings, conducted by Blue Cross-Blue Shield's Member Relations Department, which is a part of the Education Division.

Nearly 90 meetings are conducted with members each year. The purposes of this program are two fold:

I. First, these meetings are a direct means of informing members about benefits in an effort to help them better understand the problems of financing health care and the local responsibility in solving them.

II. A second goal of the meetings is to provide members with a channel of expression. The reactions they have concerning benefits and their suggestions regarding future needs furnish Blue Cross-Blue Shield with a direct report on the members' thinking at the "grass roots" level.

These meetings function at three levels—local, district and state. At the local level, approximately 70 Group Leader meetings are held throughout the state each year. Presently, over 2,000 group representatives participate in this program each year.

District Member Council meetings are conducted each spring in nine areas, which include every Kansas county other than Johnson and Wyandotte. These are designed for Farm Bureau and non-group members. The present invitation list includes more than 1,000 persons who have a special interest in Blue Cross-Blue Shield and have indicated that they want to participate in the Member Council Program.

What Do Members Say?

What *do* members think? What are people saying and what do they want done? What is Blue Cross-Blue Shield doing in its educational program to answer the main questions members raise?

The following discussion of subjects commonly brought out in the meetings would probably be of interest to physicians:

Cost

Many members feel that Blue Cross-Blue Shield costs too much. Why do rates continue to rise and why can't costs be stabilized—are two commonly encountered questions.

Blue Cross-Blue Shield's Answer

Blue Cross-Blue Shield points out what hospital-medical costs *really* involve—what can be expected

if a member goes to the hospital, what factors are involved to increase the expense of adequate health care. The importance of a health program which increases benefits as costs increase is stressed, while the dangers in a program carrying fixed rates *but* also maintaining fixed benefits is pointed out. The fact that the cost of hospital-medical care is not too high in relation to amounts spent for other consumer items is illustrated.

Misuse

Quite often members have the impression that hospitals and physicians take advantage of Blue Cross-Blue Shield.

Blue Cross-Blue Shield's Answer

Clearing up such misconceptions involves the careful explanation of the activities followed by physicians, hospitals, and Blue Cross-Blue Shield in the careful spending of the benefit dollar.

Members are reassured that charges by hospitals and physicians to Blue Cross-Blue Shield members are the same as to non-members. Information about the continuous hospital auditing program is conveyed. Members are told about fee surveys and of the continuing collection of data regarding health care costs carried on by the Plans. The work of Utilization Study Committees is described.

Benefits That Interest Members

- A substantial number of members are very interested in the Diagnostic X-ray Rider. At the present time, this coverage is available only to the members of Employee Groups.
- Members want more optional benefits. They like the idea of wide ranges in choices to fit a variety of need. Here again, the various optional benefits are available only for Employee Group selection.
- Members hope for better benefits for people over 65. They especially are concerned with more comprehensive ranges of coverage for those now 65 and over who have been members for many years with little or no utilization. This is an area to which Blue Cross-Blue Shield has given a great deal of study, but at the present time coverage is still limited for people 60 years of age and over.

In meetings, Blue Cross-Blue Shield encourages suggestions and ideas from members on the subject of getting the highest coverage possible at a cost that is acceptable. Members are urged to upgrade benefits, and the need for selecting more comprehensive coverage is made clear.

Benefits That Do Not Interest Members

- Most members are *not* interested in increasing deductibles in Blue Cross.
- A high percentage of members would resist any forced increase in benefits. They are convinced that holding the line on costs dominates member attitude toward health prepayment, especially among younger people with families. They prefer varied optional offerings.
- Blue Shield Schedule 2 is still not attractive to many members. However, they *do* have interest in programs that provide predictability of coverage. They feel less opposition to an increased cost which would result in such a plan. In this area, a new Service Benefit program (designated as Schedule 3) has been introduced in three counties—Butler, McPherson, and Montgomery—and has been very well accepted. Other counties have plans for introducing this new Service Benefit program in the fall.

These are some of the most significant excerpts from member thinking in recent Member Council meetings. The approaches to correcting member misconceptions, as outlined above, are commonly employed by Plan representatives during discussions on these points.

Blue Cross-Blue Shield's educational efforts are aimed at goals of better understanding, benefit upgrading and membership retention. The "grass root" contacts embodied in educational meetings with members furnish a foundation for the broader approaches employed in publications and other mass media of communication.

Kansas Press Looks at Medicine

(Continued from page 372)

probably require a state constitutional amendment, a rather laborious process. Apparently public and official interest in the problem is too slight to accomplish this much-needed improvement in local government.—*Wichita Evening Eagle and Beacon,* June 23, 1961.

Love the soil. The work is hard and sometimes the return is little . . . but you will find in the good earth and fields a sure refuge from dangerous materialism.

Pope John XXIII

By doing . . . convincing things conviction is carried and results achieved that can never be accomplished by explaining them.—*Edward Steichen*

Spiritual life and secure life do not go together. To save oneself one must struggle and take risks.

—Ignazio Silone

Kerr-Mills Versus King-Anderson

The AMA has been accused of being "against"—Actually—that organization and all of its members are as anxious for the aged and all people to have the best medical care possible, as are the politicians who are looking only for votes and tax money from you and me. We are against auto accidents and burns from firecrackers as well as many other things including government control and government compulsion. Politicians and some news agencies accuse us of being against the 4th of July because we oppose fireworks. This is the typical approach of some politicians to get votes.

For more than twenty years the question of adopting some kind of National program for the medical care of the American people has been before Congress. The Wagner-Murray-Dingle bills, presented first in 1943, had they passed, would have established compulsory health insurance for all the citizens of this country. All members of the medical profession along with dentists, lawyers, insurance companies, and many others, fought this legislation and it was not passed.

In 1960, with the support of the medical profession, Congress passed the Kerr-Mills bill which is now the law of the land. This was in recognition on the part of the AMA that a small segment, and I use the word advisably, of the sixteen and one-half million people in the United States who are 65 years of age or over need health care. The proponents of Forand type legislation, now known as King-Anderson, intimate that all sixteen and one-half million are sick, all too poor to pay for health care and intimate also that they live in hovels unfit for human habitation.

These following statistics have been established by a group of sixteen professors from fifteen different colleges under Professors J. W. Wiggins and H. Schoeck, of Wayne University. This is the most honest means test ever done and reveals salient facts.

1. The average annual income of the aged is between two and three thousand dollars.

2. Cash equivalent assets over liabilities are in excess of $10,000.

3. 33.6 per cent are still working.

4. 25 per cent live with their children.

5. 64 per cent have some kind of voluntary health and hospital insurance.

6. 96 per cent owed no money to hospitals, drug stores, dentists or doctors.

Does it appear from this that all 16½ million need to be put under a blanket of limited care? I am convinced that if 16½ million Americans 65 years of age or over were carefully informed concerning the King-Anderson legislation and its cost to their children in taxes, the majority would vote against it if the opportunity were given them to do so. Much is said and will be said by the proponents of Social Security medical care about the increased cost of the care of the sick and injured. These costs have increased, but so have all costs. Let us show what the U. S. Department of Commerce has said concerning cost increases in 20 years up to 1959 which are the only figures available.

At the close of 1959, the U. S. Department of Commerce Office of Business Economics produced figures showing percentage increase of various elements of life in these United States as well as where today's dollar goes.

The U. S. Office of Business Economics, admitting that all costs are higher today than ever, offer an interesting comparison of the advances in prices over a twenty-year period. The American dollar is spent in the following ratios according to their survey:

Twenty-seven per cent for housing, 22 per cent for food, 12 per cent for travel, 6 per cent for recreation, 10 per cent for clothing, *6 per cent for health,* 5 per cent for tobacco and liquor, 12 per cent for all other items.

Now the comparative percentage advance in costs is even more revealing. Over the twenty-year period, cost of domestic servants has advanced 297 per cent, food costs up 151 per cent, shoes 169 per cent, clothing up 106 per cent, physicians fees only 90 per cent higher than twenty years ago. Health bills are higher but not as much higher as most other things purchased with our presently inflated dollar.

Twenty years ago the physician received 30 per cent of the health dollar; today it is 25 per cent. The drugs took 22 per cent twenty years ago; now 20 per cent. Hospital costs as well as health insurance are both higher today.

These comparisons show that Americans are paying less for health today than they did twenty years ago and are receiving the highest quality medical service available anywhere in the world.

Kerr-Mills bill is now the law of the land. It was proposed by Democratic Senator Robert Kerr and Representative Wilbur Mills of Arkansas, also a Democrat. It was supported by the AMA and its members.

I repeat: There is no organization or group of people more concerned about the health of all people than the American Medical Association and its members. The greatest amount of its resources, in money as well as its multiple committees and councils, is devoted entirely toward improving the care of the sick and injured and the education of doctors of medicine for that purpose and for research. The health record of these United States is ample testimony for the efficiency of this system.

What would the Kerr-Mills bill accomplish in the care of those elderly people?

It would enable the individual states to guarantee to every aged American—*who needs help*—the health care he requires—the two million Americans now covered by old age assistance and all other older persons who could not meet the cost of serious or protracted illness.

It should be noted that the Kerr-Mills law has two parts. *Part I* has to do with persons on Old Age Assistance and is referred to as "OAA." *Part II* provides for health care for persons over 65 who are *not* on relief but who need help with their medical expenses, and is referred to as Medical Assistance to the Aged ("MAA").

The Federal Government would grant funds to the states on the basis of per capita income and the services each state elected to provide. The states and local communities would decide eligibility and amount needed. This law specifies "Inpatient hospital or clinic services, home health care services, private duty nursing services, physical therapy and related services, dental services, laboratory and x-ray services, prescribed drugs, eye glasses, dentures, prosthetic devices, diagnostic screening and preventive services and any other remedial care recognized under state law.

How would all of this work in Kansas?
Old age assistance, this year's budget:

State pays	$1,422,600.00
County	2,436,887.00
	3,859,000.00+

There are four other categories receiving aid but in the aged group the federal government adds approximately an equal amount.

Under the Kerr-Mills law, the federal government would pay 57.52 per cent while the state will pay 42.48 per cent. The program would be administered through the State Board of Social Welfare and the County Welfare Department. These agencies are politically appointed or elected in our own state or county. Thus, the administration is already set up and is close enough to be under the critical eye of the vendors of material and services and also the individual tax payers.

To implement the program in Kansas, our legislature would need to appropriate a definite sum based on the needs of 128,000 aged. Of these, about 28,000 are on relief (OAA) and come under Part I; the remainder (100,000) belong under Part II (MAA). No more than one-fourth, or 32,000, could possibly need medical care during a year. It has been estimated that Kansas would need to appropriate six million new tax dollars and that the total cost would not exceed 14 million dollars. This to be administered by the state and local communities. Our state and county expenditure on welfare, exclusive of federal participation, this year will be $6,316,291.10.

Let us now examine the King-Anderson legislation as it is now in committees of Congress. It is designed to raise social security tax to 3¾ per cent of wages on a base of $5,000 in 1962 and other annual raises up to 4¾ per cent by 1968. Remember this is really only half of the tax since the employer shares equally. You are not so naive as not to know who actually will pay this bill—the consumer of goods and services, of course. Politicians—being what they are—give no assurance against further raises. Is there any tax base remaining unchanged? The answer is *NO!* and changes always upward.

The sole administrator of this huge sum of money is the Secretary of Health, Education, and Welfare, who is appointed by the President—there should be no need to go further to connect this program to Federal politics, regardless of the party in power. In addition, however, there is to be a council of 14, also appointed, to help implement the program, and

these individuals are to receive $100.00 per day plus expenses when they work.

It is our firm opinion that politics and medicine do not mix. King-Anderson legislation gives free choice of physician on the part of the patient—provided—that physician has signed a contract with the Federal Bureau. The benefits thus far allowed are more limited than Kerr-Mills legislation. Here are a few other objections which we believe are pertinent.

1. The cost would be astronomical. Much of this would go for administration of the program under Social Security.

2. It is *unnecessary* because last September 13 the Kerr-Mills bill was passed and should be given an opportunity to prove its worth.

3. In our opinion it would mean poorer, not better, health care for the aged. Psychosomaticism would increase tremendously. Imaginary pains can become real to some people who know that a soft bed, daily bath and meals served in bed lie at the other end of a protracted illness.

4. It would lead to the decline, perhaps the end, of private, voluntary health insurance.

5. In our opinion, that which would start out as health care of the aged would mushroom into socialized medicine for the entire population thus ending another segment of free enterprise.

6. Even though it would spread the cost of illness among all wage earners, it is taxation without representation.

7. It would be another political football changing with administrations and congresses and always with more and more controls.

Lenin said that the Key Stone of the Arc of Compulsion is in the care of the sick. King-Anderson legislation is a foot in the door of socialism. It is not Social Security which pays people money with which to purchase what they want and need when they retire. It is a promise of a limited amount of service to an increasing number of people at a cost dictated by a Federal Bureau.

The doctors of America believe that every person in need of medical service should get it whether he or she can afford it or not. We also believe in helping only those who need help.

President Kennedy said in his inaugural address, "We must not ask, What can my country do for me, but rather, What can I do for my country?"

Finally, when a maximum of freedom has been achieved, as it has in America, it is threatened by ideologies that are intrinsically destructive of freedom, then the liberal is a conservative dedicated to maintain and defend the cause of liberty.

L. S. NELSON, SR., M.D.
Salina, Kansas
Chairman, Committee on
Public Relations

State Hospitals

(The Division of Institutional Management of the State Board of Social Welfare prepared a statement of the functions and admission procedures of the eleven state institutions under its direction. This information will be published serially during the next several months.—Ed.)

The *Kansas Treatment Center for Children* is the children's section of Topeka State Hospital, providing psychiatric treatment for emotionally, mentally and socially disturbed children under 16 years of age. Currently, thirty beds are available for children between the ages of 6 and 12, and approximately sixty beds for children between the ages of 12 and 16. Outpatient services are also provided, but capacity is limited by available staff time.

The statutory charge for care and maintenance of a child at the Kansas Treatment Center for Children is $28.00 per week, payable by the parent or guardian of such child. No child shall be denied the services of the institution, however, solely because of the inability of his parent or guardian to pay.

Admission forms may be obtained from county directors of social welfare, or from the Division of Institutional Management, and must be signed by the parent or parents of the child, or by his legal guardian. Each application shall be accompanied by a certificate signed by a psychiatrist or physician stating that, in his opinion, study or treatment at the institution would be beneficial to the child. The county welfare department of the county in which the child resides shall provide a social history to accompany the application for admission.

INSTITUTIONS FOR THE MENTALLY RETARDED

Kansas has three institutions for the mentally retarded or deficient: Parsons State Hospital and Training Center, Parsons; Winfield State Hospital and Training Center, Winfield; and Kansas Neurological Institute, Topeka.

Persons who have lived in Kansas for one year continuously immediately prior to application may be admitted to one of the three institutions. The residence of a child shall follow and be the same as his parents.

The Parsons State Hospital and Training Center operates a psychiatrically-oriented treatment and training program for ambulatory persons who are mentally retarded with an I.Q. below 50, who are six years of age, but not over 21 years of age.

The program at Winfield State Hospital and Training Center is directed toward the treatment and training of mentally retarded very young children, older people and multi-handicapped patients. Ambulatory persons who are mentally retarded with an

I.Q. below 50 and who are over two years of age and under six, or who are over 21 years of age; or non-ambulatory persons or multi-handicapped persons of any age who are mentally retarded with an I.Q. below 50, may be admitted.

The Kansas Neurological Institute, which is cusrently being activated, will admit persons who are mentally retarded with an I.Q. below 50, who are between the ages of two and 21. Plans are under way to develop a vocational rehabilitation unit at this institution.

Infants under two years of age, showing signs of severe mental deficiency, are not admitted unless in addition they have obvious malformations and deformities. Children with an I.Q. between 50 and 70 are eligible for admission to an institution for the mentally retarded only if they require evaluation, treatment or training not provided by special classes in the public schools.

Determination as to which of the three institutions an application is to be referred, will be made by the Division of Institutional Management in cooperation with staff of the respective institutions, and based upon the evaluation, treatment and training needs of the applicant as well as available facilities within the institutions. Transfers of patients among the three institutions may be made subject to the approval of the State Director of Institutions when it is considered in the best interests of the patient.

Outpatient services for evaluation are currently available only on a very limited basis due to demands on staff time for inpatient services.

Application forms for admission are available from county directors of social welfare, and must be signed by parents, legal guardian, or spouse of the person for whom application is made. The application also requires the signed statement of a physician indicating that in his opinion the applicant is mentally deficient, and would benefit from the program of the institution. A report of psychological testing, if such testing has been done, and a complete social history of the applicant and his family must also accompany the application.

Charges for care and treatment are explained under "State Hospitals for the Mentally Ill."

Tuberculosis Hospitals

Hospital care for tuberculosis patients is provided at the Southeast Kansas Tuberculosis Hospital, Chanute, Kansas, if the person needing treatment is from one of the eighteen southeast Kansas counties; or at the State Sanatorium for Tuberculosis, Norton, Kansas, if the patient resides elsewhere in Kansas. Outpatient diagnostic and treatment services are also provided at Chanute and Norton.

Application forms for admission to the state tuberculosis facilities may be obtained from county directors of social welfare, and must be signed by the applicant or guardian and his physician. The physician's statement based upon examination of the applicant, recommends admission to a tuberculosis sanatorium or hospital.

Persons who have lived in Kansas for one year continuously immediately prior to application, may be admitted, provided that the residence requirement may be waived in cases where residence cannot be ascertained or where a medical emergency exists.

A tuberculosis patient, or person suspected of having tuberculosis, may be committed by the court to a state sanatorium for tuberculosis, and may be restrained from leaving such sanatorium, if he is found guilty of failure, or refusal to follow orders and instructions of the health officer in regard to examination and treatment.

At the tuberculosis facilities, a charge of up to $12.00 per day is made for hospitalization. No patient is refused hospitalization or outpatient services because of inability to pay.

Patients hospitalized with schizophrenia, the nation's number one mental disorder, stay in mental hospitals almost one and a half times longer than other mentally ill persons, according to the March issue of *Patterns of Disease,* a monthly Parke, Davis & Company publication for physicians. Average hospital residence of a schizophrenic is 10.8 years, compared with 7.5 for patients with other mental disorders.

However, many schizophrenic persons with symptoms not severe enough to warrant hospitalization are treated by physicians other than psychiatrists. Today, 8 of 10 of these patients need not be institutionalized, according to *Patterns.*

If we are to succeed in the great struggle of ideas that is under way, we must first of all know what we believe. We must also become clear in our minds as to what it is that we want to preserve. . . .

—*Friedrich A. Hayek*

Monotony is the law of nature. Look at the monotonous manner in which the sun rises. . . . The monotony of necessary occupations is exhilarating and lifegiving.—*Gandhi*

A truly appreciative child will break, lose, spoil, or fondle to death any really successful gift within a matter of minutes.—*Russell Lynes*

It takes patience to appreciate domestic bliss; volatile spirits prefer unhappiness.—*George Santayana*

Book REVIEWS

CONGENITAL MALFORMATIONS, edited by G. E. W. Wolstenholme and C. M. O'Conner for the Ciba Foundation, Little, Brown, and Co., Boston, 300 pages, $9.00.

The volume incorporates 12 papers on the subject together with much well-edited discussion by 29 participants from a symposium held in January, 1960. The control of many of the diseases of early childhood recently directed attention at the little known field of teratology at the early extreme of childhood. Chemical, physical, as well as microbial factors may have essentially a three-fold effect, first, an effect on a chromosome with the genetic defect being apparent in the fetus (either early or later in life, such as with Klinefelter's syndrome), secondly, a direct chemical effect on the fetus, and thirdly, there may be an effect on the placenta, which is reflected in the fetus. The latter two may also be mediated by vitamin deficiency. L. S. Penrose and C. E. Ford amongst others discuss mongolism, pointing out that additional autosomal chromosomes had been found for numbers 15, 17, or 21 and that these arose accidentally in older mothers in only about 80 per cent of instances, whereas in 20 per cent this malformation is transmitted familially independent of maternal age. Ingalls examines environmental factors, constituting different risks to fetuses at different ages, relating to cataracts, heart defects, cleft palate, mongolism, and deafness, all due to insults occurring between the fifth and the ninth week of gestation through a variety of teratogenic agents such as rubella, influenza, and maternal hypoxia, etc. A number of investigators deal with experimental models, primarily mice and rats, where a number of anti-neoplastic cytostatic drugs such as nitrogen mustard, myleran, triethylene melamine, actinomycin D and aminopterin have been found to produce a variety of fetal malformations, if litters are not resorbed. Some of the patterns of malformation are rather consistent and others are quite variable. The effects of vitamin A deficiency, thyroxin and X-irradiation are discussed, from animals, giving a survey of the range of effect that might be observed in man. In addition, the causes and morphogenesis of certain clinical syndromes are discussed, such as congenital runts, anencephaly, hydramnios, pre-diabetes and hypothyroidism. The symposium appears to cover the field rather comprehensively except for progesterone and its androgenic degradation products which are insufficiently discussed. The volume presents a good introduction to this rapidly growing field.—*J.K.F.*

FRENCH'S INDEX OF DIFFERENTIAL DIAGNOSIS, 8th Ed. A. H. Douthwaite, Editor, 1111 pages, $24.00. The Williams & Wilkins Co., Baltimore, exclusive U. S. Agents.

This newest (8th) edition of *French's Index of Differential Diagnosis* is characterized by the deletion of obsolete material and the eradication of excessive cross-references, and at the same time new symptom-complexes and hitherto unrecognized diseases have been carefully integrated into the standard references. The entire scope of modern medical knowledge has been compressed into a single reference, simple enough for the student to use as a text, yet detailed enough for the most exacting clinician to profit by its use.

While the print is smaller than that found in the usual text, still it is clear and readable and the illustrations have been selected with unusual care. Few books on the physician's shelf will provide greater reward in their day to day use.—*G.L.T.*

FUNCTIONAL ANATOMY OF THE LIMBS AND BACK—A TEXT FOR STUDENTS OF PHYSICAL THERAPY AND OTHERS INTERESTED IN THE LOCOMOTOR APPARATUS, second edition, illustrated. W. Henry Hollinshead, Ph.D., 403 pages, $5.50. W. B. Saunders Co., Philadelphia, 1960.

This is a well designed book for all those who are interested in physical medicine. It is concise, clear, and above all logically presented. The illustrations are chiefly line drawings, unincumbered by details. In many respects the practicing physician will find this most useful for a thorough run-down on the extremities and back.—*P.G.R.*

Obituaries

VICTOR E. CHESKY, M.D.

Dr. Victor E. Chesky, 76, physician and surgeon of Halstead, died June 22 of coronary occlusion at the Halstead Hospital. At the time of his death he was Chief of Surgery and President of the Hertzler Research Foundation.

He received the M.D. degree from Northwestern University Medical School in 1915. He interned at Kansas City General Hospital, following which in August, 1916, he became an early associate of the late Dr. Arthur E. Hertzler at the Hertzler Clinic and the Halstead Hospital. During his 45 years in Halstead, he served as Associate and later as Chief of Staff of the Hertzler Clinic and President of the Board of Directors.

He is survived by his widow, Emma, three children and 10 grandchildren.

DALE D. VERMILLION, M.D.

Dr. Dale D. Vermillion, 56, Goodland physician specializing in eye, ear, nose and throat, died June 12 after a three week illness.

Dr. Vermillion was born July 24, 1904 in Tescott, Kansas. He attended Kansas University and the Harvard School of Medicine. He took his internship at the Rhode Island Hospital at Providence.

In addition to being an active member of the Methodist Church, Dr. Vermillion gave much time to civic organizations.

He is survived by his wife, Mary, two sons, one daughter and four sisters.

Personalities—IN KANSAS MEDICINE

Dr. Fred J. McEwen, Wichita, Governor for Kansas, of the American College of Physicians, and **Dr. J. Walker Butin,** Wichita, were among those attending the recent meeting of the American College of Physicians, at Miami.

Dr. Butin also attended the American Gastroenterological Association meeting in Chicago, May 25-27.

Drs. A. E. Cooper, Walter Stephenson, F. D. Kennedy, Norton, and their wives attended the Northwest Medical Society meeting on June 18.

Dr. Paul L. Nelson has completed his residency training in pediatrics. He returned to Concordia July 1 to join the Gelvin-Haughey staff of doctors.

Among those attending the American Medical Association Annual Meeting in New York, from Wichita, in June were **Drs. Reals, Gsell, Wayne Hird, Thorpe.**

The doctors at the Colby Clinic have announced a new appointment to the staff of the clinic. He is **Dr. S. Paul Hornung,** a former Norton doctor and a graduate of the University of Kansas.

Dr. C. V. Haggman of Scandia was one of the 95 Kansas University alumni of 50 or more years to receive pins and membership to the Alumni Association Gold Medal Club at a reunion luncheon on June 4.

Dr. Hugh D. Riordan, Wichita, attended the Third World Congress of Psychiatry in Montreal, and the meetings of the American EEG Society, the American Neuropathology Society, and the American Academy of Neurology in Atlantic City.

Dr. Don George has ended his practice of medicine in Salina. Dr. George left for the Cherokee Mental Health Institute, Cherokee, Iowa, where he begins a 3-year residency in psychiatry.

Dr. and Mrs. John J. Chung left Sharon Springs, June 20 for New York City to attend the American College of Chest Physicians annual meeting. Dr. Chung took some postgraduate work in diseases of the chest while attending the meeting.

NEW MEMBERS

The JOURNAL *takes this opportunity to welcome these new members into the Kansas Medical Society.*

Ira Cox, Jr., M.D.
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Mission, Kansas

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1. Youmans, J. B.: Am. J. Med. 25:659 (Nov.) 1958

cardiac diseases "Who can say, for example, whether the patient chronically ill with myocardial failure may not have a poorer myocardium because of a moderate deficiency in the vitamin B-complex? Something is known of the relationship of vitamin C to the intercellular ground substance and repair of tissues. One may speculate upon the effects of a deficiency of this vitamin, short of scurvy, upon the tissues in chronic disease."[2] 2. Kampmeier, R. H.: Am. J. Med. 25:662 (Nov.) 1958.

arthritis "It is our practice to prescribe a multiple vitamin preparation to patients with rheumatoid arthritis simply to insure nutritional adequacy . . ."[3]
3. Fernandez-Herlihy, L: Lahey Clinic Bull. 11:12 (July-Sept.) 1958.

digestive diseases Symptoms attributable to B-vitamin deficiency are commonly observed in patients on peptic ulcer diets.[4] Daily administration of therapeutic vitamins to patients with hepatitis and cirrhosis is recommended by the National Research Council.[5] 4. Sebrell, W. H.: Am. J. Med. 25:673 (Nov.) 1958. 5. Pollack, H., and Halpern, S. L.: Therapeutic Nutrition. National Academy of Sciences and National Research Council, Washington, D. C., 1952, p. 57.

degenerative diseases "Studies by Wexberg, Jolliffe and others have indicated that many of the symptoms attributed in the past to senility or to cerebral arteriosclerosis seem to respond with remarkable speed to the administration of vitamins, particularly niacin and ascorbic acid. These facts indicate that the vitamin reserve of aging persons is lowered, even to the danger point, more than is the case in the average American adult."[6] 6. Overholser, W., and Fong, T.C.C. In Stieglitz, E. J.: Geriatric Medicine, 3rd edition, J. B. Lippincott, Philadelphia, 1954, p. 264.

infectious diseases Infections cause a lowering of ascorbic acid levels in the plasma; and the absorption of this vitamin is reduced in diarrheal states.[7] 7. Goldsmith, G A.: Conference on Vitamin C. The New York Academy of Sciences, New York City, Oct. 7 and 8, 1960. Reported In: Medical Science 8:772 (Dec.10) 1960.

diabetes Diabetics, like all patients on restricted diets, require an extra source of vitamins.[8] "Rigidly limiting the bread intake of the diabetic patient automatically eliminates a large amount of thiamin from the diet. . . . There is some evidence of interference with normal riboflavin utilization during catabolic episodes."[9]
8. Duncan G. G.: Diseases of Metabolism 4th edition W. B. Saunders, Philadelphia, 1959, p. 812. 9. Pollack, H.: Am. J. Med. 25:708 (Nov.) 1958.

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Bibliography *(13 clinical studies, 858 patients)*: **1.** Alexander, L. (35 patients): Chemotherapy of depression – Use of meprobamate combined with benactyzine (2-diethylaminoethyl benzilate) hydrochloride. J.A.M.A. 166:1019, March 1, 1958. **2.** Bateman, J. C. and Carlton, H. N. (50 patients): Meprobamate and benactyzine hydrochloride (Deprol) as adjunctive therapy for patients with advanced cancer. Antibiotic Med. & Clin. Therapy 6:648, Nov. 1959. **3.** Beerman, H. M. (44 patients): The treatment of depression with meprobamate and benactyzine hydrochloride. Western Med. 1:10, March 1960. **4.** Bell, J. L., Tauber, H., Santy, A. and Pulito, F. (77 patients): Treatment of depressive states in office practice. Dis. Nerv. System 20:263, June 1959. **5.** Breitner, C. (31 patients): On mental depressions. Dis. Nerv. System 20:142, (Section Two), May 1959. **6.** Gordon, P. E. (50 patients): Deprol in the treatment of depression. Dis. Nerv. System 21:215, April 1960. **7.** Landman, M. E. (50 patients): Clinical trial of a new antidepressive agent. J. M. Soc. New Jersey. In press, 1960. **8.** McClure, C. W., Papas, P. N., Speare, G. S., Palmer, E., Slattery, J. J., Konefal, S. H., Henken, B. S., Wood, C. A. and Ceresia, G. B. (128 patients): Treatment of depression – New technics and therapy. Am. Pract. & Digest Treat. 10:1525, Sept. 1959. **9.** Pennington, V. M. (135 patients): Meprobamate-benactyzine (Deprol) in the treatment of chronic brain syndrome, schizophrenia and senility. J. Am. Geriatrics Soc. 7:656, Aug. 1959. **10.** Rickels, K. and Ewing, J. H. (35 patients): Deprol in depressive conditions. Dis. Nerv. System 20:364, (Section One), Aug. 1959. **11.** Ruchwarger, A. (87 patients): Use of Deprol (meprobamate combined with benactyzine hydrochloride) in the office treatment of depression. M. Ann. District of Columbia 28:438, Aug. 1959. **12.** Settel, E. (52 patients): Treatment of depression in the elderly with a meprobamate-benactyzine hydrochloride combination. Antibiotic Med. & Clin. Therapy 7:28, Jan. 1960. **13.** Splitter, S. R. (84 patients): Treatment of the anxious patient in general practice. J. Clin. & Exper. Psychopath. In press, April-June 1960.

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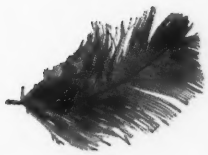

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References: 1. Santos, I. M. H., and Unger, L.: Ann. Allergy 18:172 (Feb.) 1960. 2. Charlton, J. D.: Ann. Allergy, in press. 3. Shaftel, H. E.: Clin. Med. 7:1841 (Sept.) 1960.

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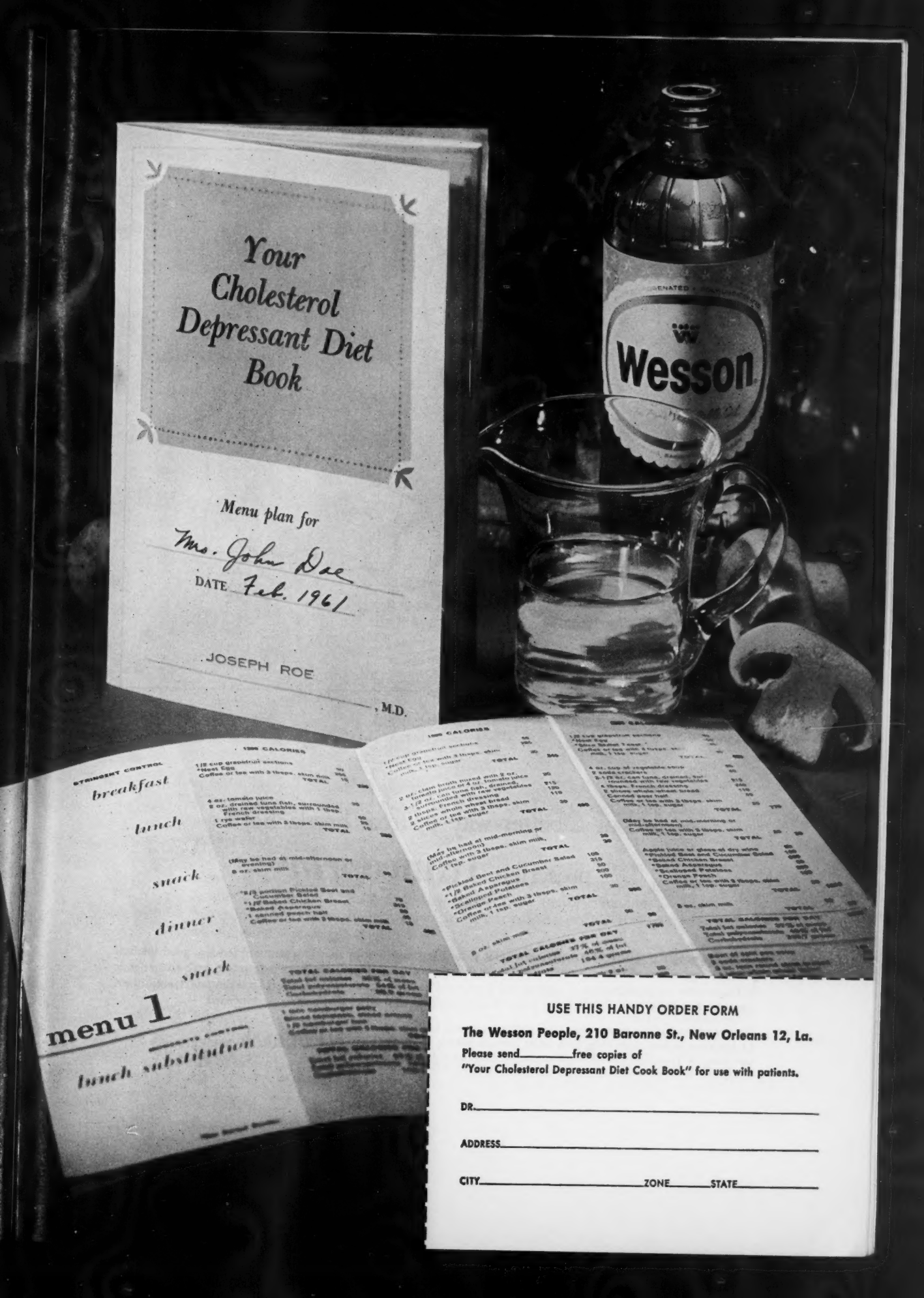

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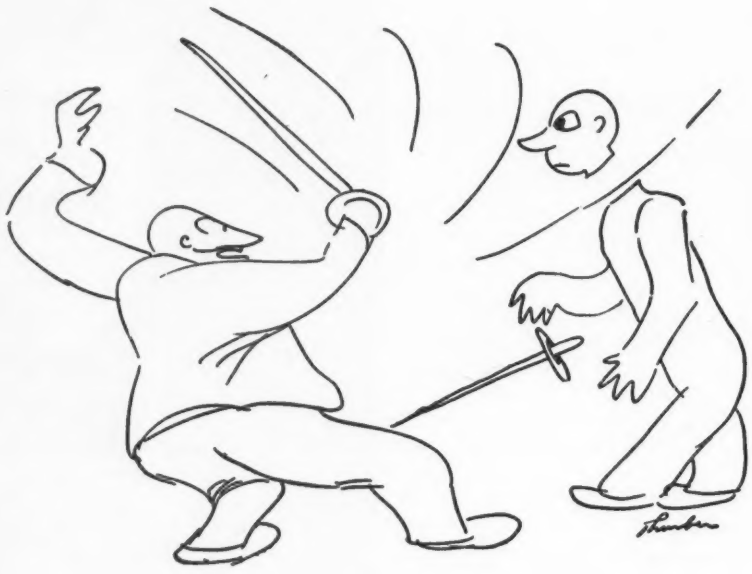

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*JAMA 163: 359,1957 (Feb. 2)

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[1]*Jorres, S. M.: Unpublished test report from Pratt Diagnostic Clinic, New England Medical Center, Boston, Mass. (July, 1958)* NW-660

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references: (1) Lish, P. M.; Albert, J. R.; Peters, E. L., and Allen, L. E.: Arch. internat. pharmacodyn. *129*:77-107 (Dec.) 1960. (2)Howell, C. M., Jr.: North Carolina M. J. *21*:194-195 (May) 1960. (3) Clinical Research Division, Mead Johnson & Company. (4) Wahner, H. W., and Peters, G. A.: Proc. Staff Meet. Mayo Clin. *35*:161-169 (March 30) 1960. (5) Crepea, S. B.: J. Allergy *31*:283-285 (May-June) 1960. (6) Crawford, L. V., and Grogan, F. T.: J. Tennessee M. A. *53*:307-310 (July) 1960. (7) Spoto, A. P., Jr., and Sieker, H. O.: Ann. Allergy *18*:761-764 (July) 1960. (8) Arbesman, C. E., and Ehrenreich, R.: New York J. Med. *61*:219-229 (Jan. 15) 1961.

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